DIAGNOSTIC PARS PLANA VITRECTOMY REPORT OF A 21-YEAR RETROSPECTIVE STUDY*

BY *George N. Palexas*, MD, (BY INVITATION) *W. Richard Green*, MD, *Morton F. Goldberg*, MD, AND *Yulan Ding*, MS[1](BY INVITATION)

ABSTRACT

Purpose: To review the experience of diagnostic pars plana vitrectomies (PPV).

Methods: The authors reviewed 405 consecutive diagnostic PPVs performed between November 1973 and October 1994.

Results: Diagnostic vitrectomy was performed in 215 (53%) of 405 eyes for suspected endophthalmitis. Of those 215 cases, acute inflammation was confirmed in 62 (28.8%), 60 (27.9%) had microbial organisms present and 36 (16.7%) were culture-positive.

Microbial organisms were observed microscopically in 31 (20%) of 156 patients suspected of postoperative endophthalmitis. Of those 31 cases, 23 (74%) were gram-positive, eleven (37%) of 30 eyes had organisms associated with glaucoma filtering procedures and 20 (16%) of 126 eyes had organisms with non-filtering procedures. The pooled percentage of eyes that developed postoperative endophthalmitis as a complication during the period July 1990 thru June 1994 is 5 (0.046%) out of a heterogeneous group of 10,898 cases operated on at the Wilmer Eye Institute for cataract, glaucoma, corneal transplant, pars plana vitrectomy and retinal detachment.

Bacteria were identified microscopically in 6 (18%) of 34 post-traumatic cases. Microbial organisms were identified in 23 (92%) of 25 cases with an endogenous infection. Patients with endogenous infections had the most fungal infections, and the majority were in males.

Neoplasms were diagnosed in 58 (14%) of the 405 cases. The most common neoplasm was ocular lymphoma 42 (72%), 69% of which were in females. Only 42 (48.3%) of 87 patients clinically suspected of having ocular lymphoma, actually had ocular lymphoma. Those negative for lymphoma were significantly older (67.4 ± 10 years) compared to those with lymphoma (60.4 ± 14 years) ($P = 0.01$).

* From the Eye Pathology Laboratory, Wilmer Ophthalmological Institute and Department of Pathology (Drs Palexas, Green, and Goldberg), and the Wilmer Eye Institute Biostatistics Center (Mr Ding), The Johns Hopkins Medical Institutions, Baltimore. Supported in part by National Eye Institute Core Grant EY01765, The International Order of Odd Fellows, and an unrestricted grant from Research to Prevent Blindness.

Conclusion: Diagnostic PPV has proved to be valuable in confirming and establishing various clinical diagnoses.

INTRODUCTION

The development of surgical techniques for excision of the vitreous, concurrently with cytopathologic techniques, has permitted the analysis of small tissue samples obtained by vitrectomy.[1-9] The refinement of this technique has allowed for determination of pathologic processes early in the course of some diseases. It has become important in confirming presumptive clinical diagnoses and the establishment of unsuspected diagnoses.[10-16]

We reviewed 405 consecutive diagnostic vitrectomy specimens obtained from 405 patients by vitreous surgery, from November 14, 1973 to October 6, 1994. The cases were categorized into six clinical groups: posttraumatic, postocular surgery, endogenous endophthalmitis, idiopathic intraocular inflammatory conditions, intraocular neoplasm, and miscellaneous.

Our objective was to determine the relative frequencies of each of the six categories over the last 21 years and to assess the demographic characteristics. The infectious agents in the posttraumatic, postocular surgery, and endogenous endophthalmitis categories were characterized microscopically and by cultures. The predisposing factors for the type of infection identified were characterized. In patients with idiopathic ocular inflammation, the type and frequency of the inflammatory cell type was assessed. The cytologic and demographic features of patients with definite ocular lymphoma and those clinically suspected of having, but microscopically negative for, ocular lymphoma were compared.

MATERIALS AND METHODS

We performed a retrospective review of all diagnostic ocular fluid specimens that were submitted to the Eye Pathology Laboratory between November 14, 1973, and October 6, 1994, for microscopic study. All specimens were obtained by pars plana aspiration and vitrectomy except one that was obtained by anterior vitrectomy. Information regarding these patients was obtained from the review of eye pathology records, Wilmer Institute medical records, and records provided by referring physicians involved in the care of the patients.

Each case was categorized into one of the 6 groups listed previously according to the clinical history and microscopic findings.

Factors determined for each category included demographic data, the hospital where the diagnostic vitrectomy was performed, the name of the surgeon, and the date of the diagnostic vitrectomy.

In specimens in which an organism was identified on microscopy, culture data were retrieved from patient records and, in some cases, from records

of the microbiology laboratory. When an organism was identified microscopically or by culture, such a patient was said to have a proven infection. Parasites were identified in 3 cases and viruses in 2 cases. The incidence of postoperative infectious endophthalmitis at the Wilmer Eye Institute was determined for the period July 1990 thru June 1994, given that the total number of cases operated on for intraocular and retinal diseases was 10,898. This consisted of 4,986 cataract extractions, 1,408 glaucoma filtering procedures, 693 penetrating keratoplasties, and 3,811 retinal and vitreous procedures.

In cases of endogenous endophthalmitis and in those patients who had a clinical history and findings of idiopathic ocular inflammation, the presumptive source of infection or inflammation other than from the eye was assessed from the available records. In patients who had a history of vitreous inflammation for which a diagnostic vitrectomy was performed, the inflammation was categorized cytologically as acute, acute and chronic, chronic, and chronic granulomatous.

Forty-two cases in which a definite diagnosis of ocular lymphoma was made on cytology were compared with 42 cases that were suspected in the surgeons' previtrectomy differential diagnosis of having ocular lymphoma but were negative for it on cytology. The uses were compared for age, gender, race, laterality, and type of inflammatory cells present.

The histologic findings and inflammatory cell types representative of each of the different categories reported here have been demonstrated and described previously.[5] We report only on the percentage of inflammatory cell types present in each of the categories posttrauma, post–intraocular surgery, endogenous endophthalmitis, idiopathic ocular inflammation, and ocular lymphoma.

RESULTS

GENERAL DEMOGRAPHIC DATA

Table I lists the demographic data for the 405 patients in this series and the number of cases studied over the 21 years for each category. In the first 11 years of this study (1973 to 1984), there were only 85 cases, (21.0%) compared with 320 cases (79.0%) in the 10 years that followed (1985 to 1994). There were no differences among the categories for race and laterality.

Of the 405 vitrectomies studied, 259 cases (64%) were submitted by surgeons from the Wilmer Institute, and 146 (36%) from elsewhere. One hundred and thirty surgeons were responsible for submitting the 405 diagnostic pars plana vitrectomy specimens.

In the 215 cases suspected of infectious endophthalmitis, 62 (28.8%) had acute inflammation, 53 (24.7%) had acute and chronic inflammation, 63 (29.3%) had chronic inflammation, and 12 (5.6%) had chronic granulomatous inflammation. Vitreous was obtained by pars plana vitrectomy in

TABLE I: DEMOGRAPHIC CHARACTERISTICS OF PATIENTS WHO HAD A DIAGNOSTIC PARS PLANA VITRECTOMY

CRITERION	POST TRAUMA	POSTOCULAR SURGERY	ENDOGENOUS INFECTION	INFLAMMATORY	NEOPLASTIC	MISCELLANEOUS	TOTAL
No. of cases (N=405)	34 (8.4%)	156 (38.5%)	25 (6.2%)	103 (25.4%)	58 (14.3%)	29 (7.2%)	405
1973 - 1984	12 (35.3%)	27 (17.3%)	2 (8.0%)	7 (6.8%)	10 (17.2%)	27 (93.1%)	85 (21.0%)
1985 - 1994	22 (64.7%)	129 (82.7%)	23 (92.0%)	95 (93.2%)	48 (82.8%)	2 (6.9%)	320 (79.0%)
Gender (N=405)							
Male	29 (85.3%)	67 (43.0%)	21 (84.0%)	49 (47.6%)	22 (37.9%)	15 (51.7%)	203 (50.1%)
Female	5 (14.7%)	89 (57.0%)	4 (16.0%)	54 (52.4%)	36 (62.1%)	14 (48.3%)	202 (49.9%)
Race (N=349)							
White	27 (79.4%)	110 (76.4%)	17 (68.0%)	65 (80.3%)	31 (86.1%)	27 (93.1%)	277 (79.4%)
Black	7 (20.6%)	27 (18.8%)	7 (28.0%)	10 (12.4%)	2 (5.6%)	0	53 (15.2%)
Other	0	7 (4.9%)	1 (4.0%)	6 (7.4%)	3 (8.3%)	2 (6.9%)	19 (5.4%)
Age (yr) (N=394)							
Mean (SD)	31.4 (22.4)	66.9 (15.9)	43.4 (22.1)	59.6 (17.6)	52.4 (22.7)	45.1 (28.7)	
Range	0.3 - 82	0.5 - 93	7 - 75	10 - 88	0.5 - 82	0.1 - 89	
Laterality (N=350)							
Right	14 (46.7%)	62 (43.1%)	11 (45.8%)	36 (42.4%)	14 (34.2%)	15 (57.7%)	152 (43.4%)
Left	16 (53.3%)	82 (56.9%)	13 (54.2%)	49 (57.7%)	27 (65.9%)	11 (42.3%)	198 (56.6%)
Diagnostic vitrectomy (N=405)							
Wilmer	32 (94.1%)	127 (81.4%)	17 (68.0%)	44 (42.7%)	13 (22.4%)	26 (89.7%)	259 (64.0%)
Elsewhere	2 (5.9%)	29 (18.6%)	8 (32.0%)	59 (57.3%)	45 (77.6%)	3 (10.3%)	146 (36.1%)
No. of clinicians							
(Ratio)*	24 (1.4)	50 (3.1)	16 (1.6)	58 (1.8)	42 (1.4)	7 (4.1)	

*Ratio represents number of cases per clinician for each category.

144 instances and by vitreous aspiration in 71 of the 215 cases. Microbial organisms were observed in 6 (17.7%) of 34 posttraumatic cases, 31 (19.9%) of 156 post ocular surgery cases and 23 (92.0%) of 25 endogenous cases (Table II). Table II gives the breakdown by category and the microbiologic type of infection.

Infections were culture-proven in 36 (16.7%) of the 215 cases. Bacteria accounted for 27 of the infections and fungi for 9. Parasites including *Toxocara*, *Toxoplasma,* and *Gnathostoma* were observed in 3 cases. Virus was observed by electron microscopy in 2 cases.

POSTTRAUMA ENDOPHTHALMITIS

The 34 cases in this category represent the group with the youngest mean age (31.4 years; range, 0.3 to 82). The majority of the patients (85.3%) were males (Table I). Twenty- five (73.5%) of the patients had a history of penetrating ocular trauma (mean age, 26.9 years), 5 (14.7%) had blunt ocular trauma (mean age, 49.6 years), and 4 (11.8%) had a retained intraocular foreign body (mean age, 36.8 years).

TABLE II: MICROBIAL ORGANISMS OBSERVED IN DIAGNOSTIC PARS PLANA VITRECTOMY SPECIMENS FROM PATIENTS WITH CLINICALLY SUSPECTED ENDOPHTHALMITIS

CLINICAL CATEGORY	POSTOCULAR TRAUMA	POSTOCULAR SURGERY	ENDOGENOUS INFECTION	TOTAL
No. of cases with suspected endophthalmitis	34	156	25	215
No. of specimens with microbial organisms present	6 (17.7%)	31 (19.9%)	23 (92.0%)	60 (27.9%)
No. of specimens with micobial organisms in two periods of time				
1973 - 1984	2	8	2	12
1985 - 1994	4	23	21	48
Bacteria				
Gram-positive	3	23	4	30
Gram-negative	3	3	1	7
Mixed	-	3	-	3
Fungus	-	2	13	15
Parasite	-	-	3	3
Virus	-	-	2	2

In the 34 patients who had a diagnostic vitrectomy posttrauma, 14 (41.2%) had acute inflammation, 6 (17.6%) had acute and chronic inflammation, and 5 (14.7%) had chronic inflammation.

Bacteria were detected on microscopy in 6 (17.6%) of the 34 cases (Table II). No fungi were detected. Three cases with gram-positive and three with gram-negative bacteria were identified. Of these only 4 cases (11.8%) were culture-proven (Table IV): 1 had *Streptococcus viridans*, 2 had *Bacillus cereus*, and 1 had *Aeromonas hydrophila*.

POSTOCULAR SURGERY

This category consists of 156 cases and represents the largest group (38.5%) of the six categories. It also reflects the oldest group of patients with a mean age 66.9 years (range, 0.5 to 93). Table III lists the cases and combination of surgical ocular procedures after which a diagnostic pars plana vitrectomy was performed to exclude an exogenous cause of endophthalmitis. Of the 156 cases, 126 cases (80.8%) had ocular procedures excluding filtering surgery, and 30 cases (19.2%) had ocular procedures including filtering surgery. Of the 126 cases with no associated filtering procedure, 105 cases had cataract procedures, 11 cases had a penetrating keratoplasty, 9 retinal surgery, and 1 strabismus surgery complicated by probable scleral perforation (Table III).

Nineteen (12.2%) of the 156 cases also had a combined anterior chamber paracentesis at the time of diagnostic pars plana vitrectomy.

In the 156 patients who had a diagnostic vitrectomy for suspected endophthalmitis after ocular surgery, chronic inflammation was observed in 55 (35.3%), acute inflammation in 40 (25.6%), acute and chronic inflammation in 37 (23.7%), and chronic granulomatous inflammation in 9 (5.8%).

Microbial organisms were observed microscopically in 31 (19.9%) of the 156 cases (Tables II and III). Bacteria accounted for 29 (93.5%) of these infections, and fungi were present in two (6.5%).

No microbial organisms were observed in vitreous specimens after retinal and strabismus surgery (Table III). Twenty (15.9%) of 126 cases with microbial organisms followed some form of cataract extraction or keratoplasty with no associated filtering procedure.

Eleven (36.7%) of 30 specimens with microbial organisms followed ocular surgery, including a filtering procedure (Table III). Three of the these 11 patients (27.3%) had adjunctive antimetabolite therapy at the time of filtering surgery.

Only 20 (64.5%) cases of the 31 microscopically identified infected postoperative cases were culture-proven. This represents 12.8% of the total of 156 suspected endophthalmitis cases (Table IV). The majority of culture-proven infections were due to gram-positive organisms (18 of 20 cases, 90%). Organisms from streptococcal species accounted for 7 cases (38.9%), *Staphylococcus epidermidis* for 5 cases (27.8%), and *Staphylococcus aureus* for

TABLE III: PRIMARY SURGICAL PROCEDURES IN PATIENTS WHO SUBSEQUENTLY HAD A DIAGNOSTIC PARS PLANA VITRECTOMY FOR SUSPECTED ENDOPHTHALMITIS

TYPE OF SURGERY	TOTAL NO.	NO. WITH MICROBIAL ORGANISMS
A. Procedures with no filtering surgery	126	20 (15.9%)
Cataract surgery	105	16 (15.2%)
ECCE with PC IOL	57	6
ECCE without IOL	21	8
ICCE	12	1
ECCE with AC IOL	7	-
Phacoemulsification with PC IOL	6	1
ICCE with AC IOL	1	-
ICCE with PC IOL	1	-
Procedures with penetrating keratoplasty	11	4 (36.4%)
ECCE with PC IOL and keratoplasty	6	3
Keratoplasty	3	1
ECCE and AC IOL and keratoplasty	1	-
ECCE and phacoemulsification and keratoplasty	1	-
Retinal detachment surgery	9	-
Strabismus surgery with possible needle perforation	1	-
B. Procedures with filtering surgery	30	11 (36.7%)
Filtering surgery only	15	5
ECCE with PC IOL and filtering surgery	9	3
Phacoemulsification with PC IOL and filtering surgery	2	-
ECCE and AC IOL and filtering surgery	1	1
ICCE and filtering surgery	3	2
Total	**156**	**31 (19.9%)**

AC, anterior chamber; ECCE, extracapsular cataract extraction; ICCE, intracapsular cataract extraction; IOL, intraocular lens; PC, posterior chamber.

1 case (5.5%) of the 18 culture-proven gram-positive intraocular infections. Of the gram-positive bacterial infections, staphylococcal species were cultured in 9 (50%) of 18 cases, and streptococcal species in 7 (38.9%) of 18 cases. The only gram-negative organism isolated was *Pseudomonas aeruginosa*. Fungal endophthalmitis accounted for 1 of the culture proven cases *(Candida parapsilosis)*.

ENDOGENOUS ENDOPHTHALMITIS

This category of 25 cases represents the smallest group of patients (6.2%) of the six categories studied, with a mean age of 43.4 years (range, 7 to 75) and

TABLE IV: CULTURE-PROVEN ISOLATES FROM VITREOUS SPECIMENS FOUND MICROSCOPICALLY TO HAVE MICROBIAL ORGANISMS FROM PATIENTS WITH CLINICALLY SUSPECTED ENDOPHTHALMITIS

CLINICAL CATEGORY	POSTOCULAR TRAUMA (N=34)	POSTOCULAR SURGERY (N=156)	ENDOGENOUS INFECTION (N=25)	TOTAL (N=215)
Bacteria	4	19	4	27 (12.6%)
Gram-positive				
Streptococcal species	1	7	2	
Streptococcus pneumoniae	-	3	1	
Streptococcus viridans	1	2	-	
Group B streptococcus	-	1	-	
Group G streptococcus	-	1	1	
Staphylococcus aureus	-	1	1	
Staphylococcus epidermidis	-	5	-	
Bacillus cereus	2	-	-	
Propionibacterium acnes				
Coagulase-negative staphylococcus	-	3	-	
Enterococcus faecalis	-	2	-	
Listeria monocytogenes	-	-	1	
Gram-negative				
Pseudomonas aeurginosa	-	1	-	
Aeromonas hydrophila	1	-	-	
Fungus	-	1	8	9 (4.2%)
Candida				
Candida albicans	-	-	2	
Candida parapsilosis	-	1	-	
Candida species	-	-	2	
Aspergillus				
Aspergillus fumigatus	-	-	1	
Aspergillys flavus	-	-	1	
Cryptococcus neoformans	-	-	1	
Pseudallescheria boydii	-	-	1	
Parasite*	-	-	3	3 (1.4%)
Toxoplasma gondii	-	-	1	
Gnathostoma spinigerum	-	-	1	
Toxocara canis	-	-	1	
Virus*	-	-	2	2 (0.9%)
Cytomegalovirus	-	-	1	
Herpes zoster virus	-	-	1	
No. with culture-proven infection	4 (11.8%)	20 (12.8%)	12 (48.0%)	36 (16.7%)
No. with microbial organisms observed microscopically	4 (11.8%)	20 (12.8%)	17 (70.8%)	41 (19.1%)

*Not cultured.

the second highest percentage of males of all the categories (84%) (Table I).

In the 25 patients who had a diagnostic vitrectomy for suspected endogenous endophthalmitis, the type of inflammation was acute and chronic in 10 cases (40%), acute in 8 (32%), chronic in 2 (8%), and chronic granulomatous in 3 (12%). Twelve of the 25 suspected cases were culture-proven.

Table V lists the presumptive sources of endogenous endophthalmitis in this category. The most common associated condition was intravenous drug abuse.

Three (12%) of the 25 cases had a retinal biopsy at the time of diagnostic pars plana vitrectomy. Organisms observed were *Toxoplasma gondii*, cytomegalovirus, and herpes zoster virus in one case each (Tables II and IV).

Organisms identified in the 23 cases were fungus in 13 (56.5%), bacteria in 5 (21.7%), parasites in 3 (13%), and viruses in 2 (8.7%) (Table II).

IDIOPATHIC OCULAR INFLAMMATION

This category of 103 patients represents the second largest category of pa-

TABLE V. CONDITIONAS PREDISPOSING SUBJECTS TO ENDOGENOUS INTRAOCULAR INFECTION AND IDIOPATHIC INFLAMMATION

CONDITION	ENDOGENOUS INTRAOCULAR INFECTION	IDIOPATHIC INTRAOCULAR INFLAMMATION
Total no. of subjects	25	103
Infections		
Gastrointestinal abscess	2	1
Urogenital tract infection	-	1
Cellulitis	2	3
Meningitis	1	-
Liver abscess	-	1
Enterocolitis	1	-
Pneumonia	1	-
Hickman catheter	1	1
Esophageal Ulcer	-	1
Infections with AIDS	1	1
Intravenous drug abuse	8*	2†
Postsurgical procedures	-	4
Unclear8	8	88

*Two cases developed human immunodeficiency virus (HIV) infections.
†One case developed HIV infrection.

tients (25.4%) and the group for which the most diagnostic vitrectomies were carried out during the period 1985 to 1994 (Table I). This category represents the second- oldest group of patients, with a mean age of 59.6 years (range, 10 to 88).

The cytologic findings in this group of patients with idiopathic inflammation include 63% with chronic inflammation, 19% with granulomatous inflammation, 15% with acute and chronic inflammation, and 3% with acute inflammation. A presumptive source for the ocular inflammation was thought to be ocular lymphoma in 33 cases (32%), but this was proved negative on cytology. In 15 cases (14.6%), a diagnosis of endogenous infectious endophthalmitis was considered in the surgeon's previtrectomy differential diagnosis on the basis of a concurrent systemic infection. No causal relationship could be established on diagnostic pars plana vitrectomy for an infection in these 15 patients, except for two patients in whom the diagnosis of Whipple's disease was confirmed. In the remaining 88 cases, the precise cause or predisposing factors for the ocular inflammation were unknown. No definitive diagnosis could be made to account for the ocular inflammation on cytology.

INTRAOCULAR TUMORS

Of the 58 cases in this category, 45 were referred from outside the Wilmer Institute. The highest proportion of females (62.1%) and second lowest number of blacks (5.6%) among the six categories (Table I) are represented in this category.

Cases with ocular neoplasms represent 14.3% of all the patients studied. Table VI lists the neoplastic conditions identified by a diagnostic pars plana vitrectomy.

TABLE VI: NEOPLASTIC CONDITIONS IN WHICH CYTOPATHOLOGIC TECHNIQUES HAVE BEEN HELPFUL IN ESTABLISHING DIAGNOSES

CONDITION	NO. OF PATIENTS
Ocular lymphoma	42
Ocular lymphoma clinically suspected*	3
Retinoblastoma	5
Leukemia	2
Leukemia excluded	1
Metastatic carcinoma	2†
Melanoma	1
Melanocytoma	1
Mycosis fungoides	1
Total	**58**

†One case has been reclassified as ocular lymphoma.
*Specimens unsatisfactory.

OCULAR LYMPHOMA

Of the 87 cases clinically suspected to have ocular lymphoma, 42 were definite ocular lymphoma, 3 were cytologically suspicious for lymphoma, and 42 were negative for lymphoma. Three cases that were clinically suspected for ocular lymphoma, but that could not be confirmed histologically because of inadequate samples, were excluded from the comparison of cases with and without ocular lymphoma.

Thirty-three of the 42 cases that were negative for ocular lymphoma were from the category of idiopathic ocular inflammation, 8 cases from the category of postocular surgery, and 1 case from the category of miscellaneous disorders. Seventy-nine per cent of the positive ocular lymphoma cases were referred for cytologic evaluation during the period 1985 to 1994. Of the 42 patients with ocular lymphoma, the average age was 60.4 ± 14 years and 69% were females; 10 (23.8%) were operated at the Wilmer Institute and in 32 (76.2%) cases, the specimens were sent from elsewhere for evaluation (Table VII).

MISCELLANEOUS

Table VIII lists the miscellaneous conditions in which diagnoses were confirmed or established by cytopathologic evaluation.

DISCUSSION

This report is a review of 405 consecutive diagnostic vitrectomies carried out over a 21-year period. There was a dramatic increase in the number of cases of diagnostic vitrectomy over the last 10 years following a report[5] that delineated the advantages and diagnostic potential of this procedure in different ocular diseases. In the first 11 years (1973 to 1984) of this study, only 85 case (21%) were studied, compared with 320 cases (79%) in the 10 years that followed (1985 to 1994).

The findings from the pars plana diagnostic vitrectomies over the last 21 years are discussed in the following sections for each of the categories.

DIAGNOSTIC VITRECTOMY FOR INFECTION

Comparison of our findings in 215 patients suspected of infectious endophthalmitis with those of other series is made difficult because some published series represent a collection of data from clinically suspected cases of endophthalmitis where no invasive procedure had been carried out to confirm the diagnosis,[17] and no cultures had been attempted.[18] Also, in some series, an invasive procedure has been carried out to establish a microscopic or culture-proven diagnosis of endophthalmitis, but procedures were not uniform because ocular fluids had been sampled either from the anterior chamber or vitreous cavity by different techniques and ports of entry; the results have often then been published collectively for all the diagnostic

TABLE VII: DIAGNOSTIC PARS PLANA VITRECTOMY FOR SUSPECTED OCULAR LYMPHOMA: COMPARISON OF FEATURES IN PATIENTS FOUND TO HAVE LYMPHOMA WITH THOSE WHO WERE NEGATIVE FOR LYMPHOMA

VARIABLE	DEFINITE OCULAR LYMPHOMA	NEGATIVE FOR LYMPHOMA	*P*
No. of cases	42	42	
By years			0.57
1973 - 1984	9 (21.4%)	6 (14.3%)	
1985 - 1994	33 (78.6%)	36 (85.7%)	
Age (yr)			0.01*
Mean (SD)	60.4 (14.0)	67.4 (10.3)	
Range	35 - 82	34 - 86	
Gender			0.26
Male	13 (31.0%)	19 (45.2%)	
Female	29 (69.0%)	23 (54.8%)	
Race			
White	24	26	
Black	0	3	
Other	3	2	
Unknown	15	11	
Laterality			0.26
Right eye	8	14	
Left eye	22	18	
Unknown	12	10	
Diagnostic vitrectomy			0.34
Wilmer	10	15	
Elsewhere	32	27	
Type of inflammation			
Chronic	13	30	0.0005*
Chronic and granulomatous	0	7	0.02*
Acute	0	0	NS
Acute and chronic	1	5	0.2

NS, not significant.
*Significant.

procedures.[11,17-31] Vitreous cultures obtained by vitreous aspiration or vitrectomy in patients suspected of endophthalmitis have been shown to have different diagnostic sensitivities.[16] Isolating causative organisms obtained by performing a vitrectomy and culturing the cassette fluid provided a significantly higher yield of culture-proven endophthalmitis (76%) than simply culturing the vitreous obtained by aspiration (43%) from the same patients ($P < .01$).[16]

Our series is a report on vitreous obtained from the pars plana vitrectomy approach in all cases except one. There is no means by which we can determine in such a retrospective study what proportion of the specimen was

TABLE VIII: MISCELLANEOUS CONDITIONS IN WHICH THE DIAGNOSES WERE CONFIRMED OR ESTABLISHED BY CYTOPATHOLOGIC EVALUATION

CONDITION	NO. OF PATIENTS
Epithelial ingrowth	10 (34.5%)
Persistent hyperplastic primary vitreous	6 (20.7%)
Phacolytic glaucoma	5 (17.2%)
Amyloidosis	2 (6.9%)
Blood-induced glaucoma	4 (13.8%)
Asteroid hyalosis	1 (3.4%)
Hemoglobin spherulosis of vitreous	1 (3.4%)
Total	**29**

submitted to microbiology for culture and to cytopathology for microscopic study, or what proportion of cases had cultures from vitrectomies collected in cassettes or cultured from vitreous obtained by biopsy or aspiration. A disparity of the quantity and quality of fluid submitted for culture compared with cytopathology, as well as factors that affect the viability, culturing, isolation, and identification of the respective organisms,[15] may account for the 8.1% difference seen in this series between the microscopically proven and culture-proven endophthalmitis.

POST TRAUMA ENDOPHTHALMITIS

Incidence

Comparative data on the incidence of infectious endophthalmitis following trauma are difficult to obtain. In a retrospective review of 82 consecutive eyes with penetrating trauma seen in 1974 to 1975 at the Bascom Palmer Institute, only two culture-proven infections (2.4%) were identified.[32] In a subsequent publication from the Bascom Palmer Institute, a review of 369 cases from June 1969 to February 1985 identified 51 cases (14%) of possible infectious endophthalmitis after penetrating ocular injury. In 27 (7.3%) of the cases, the clinical suspicion of endophthalmitis was confirmed by cultures of intraocular specimens.[33]

In another study conducted over an 8-year period from January 1975 to December 1982 at the Eye Institute of the Medical College of Wisconsin, 26 (10.1%) of 257 cases of penetrating ocular trauma had suspected endophthalmitis. The incidence of culture-proven endophthalmitis was 19 (7.4%) of 257.[34]

Bacteria were observed in 6 (17.6%) of 34 vitreous specimens from eyes with suspected endophthalmitis after trauma in our series. Four (11.8%) of the 34 cases were culture-proven, and all 4 had penetrating ocular trauma.

The incidence of 13.8% of culture-proven endophthalmitis is slightly higher than in some previous studies (2.4%,[32] 7.3%,[33] and 7.4%)[34] but lower than the 30% incidence of culture-proven endophthalmitis reported for rural trauma.[35] The higher incidence of endophthalmitis associated with rural trauma may be due to an increased microbial inoculum from contaminated penetrating objects, more extensive lacerations, or more virulent organisms.[35] The population in our study was urban-based, and the incidence of 13.8% in our series of nonrural traumatic culture-proven endophthalmitis is similar to the incidence of 11% for nonrural culture-proven endophthalmitis reported by Boldt and associates.[35]

Microbiology

Bacillus cereus, a member of a genus of aerobic, spore-forming gram-positive bacilli, which is found in soil, air, water, and dirt, causes a rapid and severe endophthalmitis. It is said to be one of the most destructive bacterial organisms to affect the eye[33,35-37] and accounted for 2 of 4 culture-proven isolates in eyes with posttraumatic endophthalmitis in our series (Table IV).

In a summary of seven studies of causative organisms in posttraumatic endophthalmitis,[38] bacillus species accounted for 20% of infections (21 of 104 cases). Two additional studies both reported a higher incidence of 46% (11 of 24 cases[35] and 6 of 13 cases).[39]

In the seven studies just cited,[32-38] *Streptococcus* species accounted for 10 (9.6%) of 104 posttraumatic endophthalmitis cases. *Streptococcus viridans* was cultured in one case in our series.

Aeromonas hydrophila, a gram-negative rod, was isolated from one of our patients. The primary habitat of *Aeromonas hydrophila* is stagnant water and nonfecal sewage, which in turn contaminates water sources. The first report of a case of purulent endophthalmitis caused by *Aeromonas hydrophila* occurred as a result of a perforating injury from a dynamite blast.[39] The second case was a corneal ulcer after trauma.[40] The third case had spontaneous endogenous endophthalmitis due to *Aeromonas hydrophila* with no apparent source.[41] Our case of culture-proven *Aeromonas hydrophila* is the second report in a perforating injury of the eye.

POST OCULAR SURGERY

Incidence

The incidence of endophthalmitis after cataract surgery at the Wilmer Eye Institute was reported as 1 (0.5%) of 200 eyes between January 1975 and December 1977 for patients who had intracapsular cataract extraction,[42] and 2 (0.19%) of 1,041 eyes between August 1979 and February 1983 for patients who had extracapsular cataract extractions and posterior chamber intraocular lenses implanted.[43] No reports on the incidence of postoperative endophthalmitis, after any form of ocular surgery, have since been published from the Wilmer Eye Institute. In a review of 16 studies that ad-

dressed 30,656 eyes over the period 1979 to 1991 after cataract surgery, the incidence was given as 0.13%.[44] Others[45] reviewed 338,141 Medicare beneficiaries who were admitted for cataract extractions and found a 0.17% risk of endophthalmitis for intracapsular extraction and a 0.12% risk for extracapsular extraction or phacoemulsification. In a study from the Bascom Palmer Eye Institute that reviewed 30,002 cases of intraocular surgery between January 1, 1984, and June 30, 1989, Kattan and associates[26] reported incidences as follows: extracapsular cataract extraction with or without intraocular lens implantation, 0.072% (17 of 23,625 cases); penetrating keratoplasty, 0.11% (2 of 1,783 cases); secondary intraocular lens implantation, 0.30% (3 of 988 cases); and glaucoma filtering surgery, 0.061% (1 of 1,632 cases).

The total number of patients who had cataract extraction, glaucoma filtering surgery, corneal transplantation, and vitreoretinal surgery at the Wilmer Eye Institute during the period of July 1990 to July 1994 was 10,898. The pooled percentage of eyes that developed microscopically proven and culture-proven endophthalmitis as a complication was 0.0459% (5 of the 10,898 cases).

Of the 5 cases of culture-proven endophthalmitis during this period, 3 were bleb- related and occurred 2, 10, or 18 months after filtering surgery. One was after a series of procedures for congenital glaucoma, and one was after a second keratoplasty performed for *Nocardia* infection in the original corneal wound.

Three additional cases of proven endophthalmitis in the same period were patients who had their first procedure performed elsewhere. Two of these were delayed infections, one of which was proven to be due to *Propionibacterium acnes*[73].

The incidence of infectious endophthalmitis for the period July 1990 to July 1994 at the Wilmer Eye Institute is 3 (0.213%) out of 1,408 cases after glaucoma surgery, 1 (0.144%) of 693 cases after penetrating keratoplasty, and none of 4,986 cases after cataract extractions. These can be compared with the 0.13% incidence reported by Powe and associates[44] for the period 1979 to 1991 and with the 0.5%[42] and 0.2%[43] incidents for cataract surgery reported from the Wilmer Eye Institute previously.

After Cataract Extraction

In a review of 16 studies published between 1979 and 1991 that addressed 30,656 eyes, the pooled percentage of eyes that developed postoperative endophthalmitis was 0.13% (40 eyes) following standard extracapsular cataract extraction with posterior intraocular lens implantation, phacoemulsification with posterior chamber intraocular lens implantation, or intracapsular cataract extraction with flexible anterior chamber intraocular lens implantation.[44] Because of the frequency with which cataract surgery is performed in the United States, even this low proportion of eyes

complicated by endophthalmitis translates into a rather large absolute number of complications. The 0.13% occurrence of endophthalmitis implies that more than 1,300 new cases might occur in association with the more than 1 million cataract extractions performed in the United States annually.

Of the 156 cases of suspected postsurgical endophthalmitis, 105 followed some form of cataract extraction (Table III). The distribution among those who had a standard extracapsular cataract extraction with posterior intraocular lens implantation, phacoemulsification with posterior chamber intraocular lens implantation, or intracapsular cataract extraction with anterior chamber intraocular lens implantation is given in Table III.

In 16 (15.2%) of these 105 cases, microbial organisms were observed microscopically. The majority of infections were among cases with a history of extracapsular cataract extraction with no lens implant (8 [38.1%] of 21 cases), followed in decreasing frequency by cases with extracapsular cataract extraction with a posterior chamber intraocular lens implant (6 [10.5%] of 57 cases), and intracapsular extraction (1 [8.3%] of 12 cases) (Table III).

Evidence of a decrease in hospitalization for endophthalmitis between 1984 to 1987, during which time there was a mandated shift from in patient to outpatient cataract extraction, has been explained by the fact that patients who undergo surgery on an ambulatory basis are exposed to fewer or different pathogens compared with patients who remain in the hospital after surgery.[45,46] It is also possible that changes in surgical management (eg advances in operative technique, wound closure, management of intraocular irrigating fluids, antibiotic prophylaxis, and a switch to lenses with PMMA haptics rather than polypropylene haptics[27]) over the 4-year period 1984 to 1987 resulted in a significant decrease in the rate of endophthalmitis from 0.12% in 1984 to 0.08% in the 1986 to 1987 outpatient cohort ($P=.01$).[46]

After Penetrating Keratoplasty

In a nationwide analysis of 40,351 patients undergoing penetrating keratoplasty between 1984 and 1987, the rate of endophthalmitis was found to be 0.77% (311 patients),[47] which is higher than previously reported in studies assessing fewer individuals.[48-51] The risk of rehospitalization for endophthalmitis following penetrating keratoplasty was five times higher than that reported following cataract surgery, and if an anterior vitrectomy was performed at the time of penetrating keratoplasty, then there was a 1.5-fold increase of rehospitalization for endophthalmitis within 6 months of surgery compared with penetrating keratoplasty alone.[47] The results of any possible diagnostic pars plana vitrectomy were not given.[47]

In a clinicopathologic study of 72 keratoplasty eyes obtained surgically, exogenous endophthalmitis accounted for enucleation in 12.5% of these eyes.[52]

After Retinal Surgery:
The rate of endophthalmitis after retinal surgery is very low. In a study by Ho and McMeel,[53] two cases of postoperative endophthalmitis caused by *Staphylococcus epidermidis* were reported in 10,000 routine scleral buckling operations, an incidence of 0.02%. The majority of the scleral buckling operations consisted of lamellar scleral dissection, light application of diathermy to the scleral bed, solid silicone implant with an encircling band, drainage of subretinal fluid, and, in some cases, intraocular air injection. In a more recent series,[54] 11 cases (0.169%) of endophthalmitis occurred in a series of 6,500 cases of vitreoretinal surgery over a 5-year period. The incidence of endophthalmitis after explant surgery with or without drainage of subretinal fluid was 0.19% and after vitrectomy was 0.15%: 2 eyes were enucleated.

In our series there were 9 cases with a history of retinal surgery that were suspected of postoperative endophthalmitis. None were found to have a microbial organism in the diagnostic pars plana vitrectomy specimen (Table III).

After Filtering Surgery
Patients with surgically produced filtering blebs for glaucoma, or blebs resulting inadvertently following intraocular surgery, are at risk for endophthalmitis developing months or years after surgery.[32] Presumably, the infecting organism enters the eye through the bleb. The incidence of late infections in patients with filtering blebs has been estimated at 0.2% to 1.8%.[55] These figures, however, were obtained on the basis of clinical appearance in most series,[56-58] and cases not actually infected may have been included. Cases that present with features of endophthalmitis may be falsely classified as sterile if there is a negative culture of fluid obtained by anterior chamber paracentesis.[59] In such cases it is necessary to culture both the aqueous and the vitreous, since a negative anterior chamber culture may be accompanied by a positive vitreous culture in many cases.[21] The anterior chamber is a particularly poor compartment from which to recover viable organisms.[60]

In a report by Mandelbaum and associates,[61] the incidence of late-onset endophthalmitis associated with filtering blebs could not be calculated, since the population at risk could not be determined. Ten patients with this problem, however, were observed in a 2-year period in one report.[32]

In our series, 11 (36.7%) of 30 patients had suspected endophthalmitis after ocular surgery that included a glaucoma filtering procedure (Table III). Three of the 11 patients (27.3%) had adjunctive antimetabolite therapy at the time of filtering surgery. Adjunctive antimetabolite therapy, which increases the success of glaucoma filtration surgery in patients with poor surgical prognoses, is associated both clinically and histologically with a cystic thin-walled bleb.[62] Cystic thin-walled blebs, which are more common

after full-thickness filtration surgery than after trabeculectomy, are believed to be more susceptible to infection than thicker, more spongy blebs.[56,57] In a series of 229 consecutive trabeculectomies performed with adjunctive 5-fluorouracil, the overall incidence of bleb-related endophthalmitis was 5.7%,[63] which is higher than the previously reported 0.2% to 1.8% incidence of endophthalmitis without adjunctive 5-fluorouracil.[55] The incidence of endophthalmitis in patients who are pseudophakic and who had adjunctive mitomycin C at the time of filtering surgery was reported as 2.5%.[64] Endophthalmitis developed in 1% of patients who had been followed for 1 year after combined mitomycin C, trabeculectomy, and extracapsular cataract extraction,[65] and in 5% of patients who had adjunctive mitomycin C at the time of Molteno implant surgery.[66] The 2-minute intraoperative application of 0.2 mg/mL of mitomycin C was shown to be as effective as a 5-minute exposure, but the postoperative complication rate of endophthalmitis (4%) remained unaltered for the two different exposure times.[67]

In our series, risk of developing an infection was 3.07 times greater in patients who had ocular operations with associated filtering procedures than in patients who had ocular operations without an associated filtering procedure (confidence interval = 1.16, 8.10); this is statistically significant (P = .02), chi-squared test.

Microscopic and Culture Findings in Postoperative Infective Endophthalmitis

Endophthalmitis is a potentially devastating complication of intraocular surgery. The variability of preexisting flora, infectious pathogens, pathogen virulence, host defense, treatment delay, diagnostic culture yield, and therapy underlies the complexity of the problem. The mechanism of how intraocular infection becomes established is unclear. Wound leaks, transscleral sutures, filtering blebs, and vitreous wick syndromes all have been implicated. Molecular epidemiologic techniques recently have demonstrated the genetic identity of bacteria from vitreous aspirates with those of eyelid or conjunctival isolates in 82% of 17 cases of endophthalmitis.[68]

In culture-positive cases of endophthalmitis after cataract surgery, gram-positive organisms were observed in 76% of cases[32] and gram-negative organisms in up to 35% of cases.[21] *Staphylococcus epidermidis* accounted for 38% of gram-positive isolates, *Staphylococcus aureus* for 21%, and *Streptococcus* species for 11% of cases in an earlier study.[32] The coagulase-negative staphylococci are recognised as the most common causes of postoperative endophthalmitis,[69,70] followed by organisms from the streptococcal species.[71]

Phillips and associates[72] showed that pathogens in bleb-related endophthalmitis did not differ significantly from those found in postoperative endophthalmitis not associated with filtering blebs. In 11 (35.5%) of our 31 cases of postsurgical endophthalmitis, microbial organisms were identified with filtering blebs. Our findings are comparable to those of Phillips and associates,[72] who found that *Staphylococcus* accounted for 58.2% of

the culture-proven cases and *Streptococcus* for 33.3% of the culture-proven cases.

ENDOGENOUS ENDOPHTHALMITIS

Many different organisms have been shown to produce endogenous endophthalmitis, including fungi[74-76] (especially *Candida*[77-86] and *Aspergillus*[87-92] species), parasites,[93-96] bacteria,[97-101] and viruses.

The incidence of candidemia has risen steadily in the last decade, with a fivefold increase documented for tertiary care centers and large teaching hospitals.[102] *Candida* species are now the fourth most common cause of nosocomial bloodstream infection.[103]

The prevalence and degree of ocular involvement in patients with candidemia are unclear. Three previous prospective studies have reported the prevalence of endophthalmitis as 28%,[85] 29%,[82] and 0%[86] in patients with candidemia who were hospitalized. On review of the aforementioned studies, it is clear that two groups of investigators[82,85] used less stringent criteria for the diagnosis of endophthalmitis than Donahue and associates,[86] who reported a 0% incidence, and none performed a diagnostic pars plana vitrectomy to confirm or exclude microscopic or culture-proven evidence for the documentation of *Candida* endophthalmitis. Parke and colleagues[82] found "typical white fluffy retinal lesions" in 29% of 38 patients with candidemia. The extent of intravitreal extension was not reported. Brooks[85] considered patients to have endophthalmitis if Roth spots were present (in patients without known bacteremia) in his evaluation of 32 patients with candidemia. At least 2 of Brooks' 9 patients with "endophthalmitis" had Roth spots as their sole fundus lesions. The large discrepancy in the prevalence of infectious eye lesions among the studies of Donahue and associates,[86] Parke and colleagues,[82] and Brooks,[85] is attributable to the stricter criteria for the diagnosis of intraocular candidiasis in the study of Donahue and associates.[86]

In a study of 133 subjects in whom fungus infections were noted postmortem and whose eyes were studied histopathologically, only 24 patients (18%) had fungemia detected during life.[74] The most common underlying illness and predisposing factors included antibiotics (77%), malignancy (42%), and corticosteroid therapy (41%).[74] None of these patients were intravenous drug abusers or were immunocompromised by the human immunodeficiency virus (HIV). The eyes were involved in 14 (10.5%) of the 133 cases and found to be the fifth most commonly involved organ at autopsy among patients with *Candida*. Only 2 of the eyes had vitreoretinal involvement.[74]

In our study, a source or predisposing condition accounting for endogenous endophthalmitis was identified in 17 (68%) of the 25 cases (Table V). Eight (32%) of the patients were intravenous drug abusers, of whom 2 were positive for HIV. Fungal infections accounted for 13 of the 25 microscopically detected cases of endophthalmitis (Table II), of which 8 were culture-

proven (Table IV). Four (50%) of the 8 culture-proven cases were due to a *Candida* species, 1 of whom has been previously reported.[79]

Organisms identified from vitreous of cases of endogenous endophthalmitis in this series that have been previously reported include: *Aspergillus fumigatus*,[87] *Toxoplasmosis gondii*,[94] *Gnathostoma spinigerum*,[95] *Toxocara canis*,[96] and a patient with *Listeria monocytogenes* bacterial endophthalmitis.[98]

To our knowledge, only 6 previous cases of group G streptococcal endogenous endophthalmitis have been reported previously.[97,99,100] These patients had important predisposing factors, such as lymphoma, carcinoma of the prostate, facial trauma, and diabetes. The patient with group G streptococcal endophthalmitis reported here presented at age 73 years with a history of insulin-dependent diabetes mellitus, peripheral vascular disease, right diabetic foot ulcer, left index finger cellulitis, and loss of vision in the right eye. Examination revealed vision of 20/200 in the right eye and light perception in the left eye. The slit-lamp examination disclosed a 3-mm layered hypopyon in the left eye and keratic precipitates. A diagnostic pars plana vitrectomy specimen disclosed gram-positive cocci, and culture grew group G streptococci.

IDIOPATHIC INTRAOCULAR INFLAMMATION

The purpose of performing a diagnostic pars plana vitrectomy in cases of uveitis of unknown etiology was to either establish a specific diagnosis or eliminate suspected diagnoses. Examination of intraocular fluids aids in differentiating infection or malignancy from sterile inflammatory reactions,[8,104-107] and, unlike most intraocular tissues, vitreous cells are accessible to removal with little alteration of visual function.[108] In some cases where the diagnostic yield from the clinical history, physical examination, peripheral blood, spinal fluid, or diagnostic vitrectomy analysis may be low, a retinal, choroidal[109] or chorioretinal biopsy may yield added information.[110]

The cytologic findings in this group of patients with idiopathic inflammation included chronic inflammation in 63%, granulomatous inflammation in 19%, acute and chronic inflammation in 15%, and acute inflammation in 3%. A presumptive clinical diagnosis of ocular lymphoma was made in 33 cases. In 15 cases a diagnosis of endogenous microbial endophthalmitis was considered in the surgeon's previtrectomy differential diagnosis on the basis of a concurrent systemic infection. No evidence of infection was found on diagnostic pars plana vitrectomy in these 15 patients, except in 2 patients who were found to have Whipple's disease, 1 of whom has been reported previously.[111] In the remaining cases, the cause or predisposing factors for the ocular inflammation were unknown. No definitive diagnosis could be made to account for the ocular inflammation by cytology. In such a retrospective study, it is difficult to correlate the clinical, physical, and serologic findings with the cytologic findings in each case because there was lack of

uniformity in the approach to the inflammatory disease among the 58 different clinicians who submitted the 103 cases in this category (Table I). For this reason, the International Uveitis Study Group proposed certain recommendations for the evaluation of intraocular inflammatory disease, hoping that dissemination of this classification, based on anatomic criteria, will bring uniformity in describing and classifying ocular inflammatory diseases.[112]

INTRAOCULAR NEOPLASMS

Two cases were diagnosed as metastatic carcinoma (Table VI). One was clearly metastatic squamous cell carcinoma. The other case was previously reported as metastatic breast carcinoma to the vitreous[113] but was later, on review with cell marker studies, reclassified as ocular lymphoma. One patient with vitreous involvement in acute lymphoblastic leukemia and neovascularization of the optic nerve head was previously described.[114]

Ocular Lymphoma

Large-cell lymphoma of the eye is an important concern in patients with intraocular inflammatory infiltrates that persist despite therapy. This is a lethal disease, but early diagnosis and prompt treatment may improve the prognosis. The ophthalmologic manifestations of this disorder include isolated anterior uveitis,[115] vitritis,[116] retinitis,[117] multiple retinal pigment epithelium tumor detachments,[118] exudative retinal detachments,[119] papillitis,[120] periphlebitis,[120] retinal vasculitis,[121] retinal artery occlusions,[122] neovascular glaucoma,[123] and orbital involvement.[124]

In a series of 32 patients with histologically proven ocular lymphoma, the surgical cases of which are included in this study, central nervous system involvement occurred in 18 (56%), and in these patients the ocular symptoms preceded CNS symptoms.[125] The mean time between the onset of ocular symptoms and the onset of CNS symptoms was 29 months (range, 7 to 108). There was visceral involvement in 16% of patients, occurring with CNS disease in 6%. The visceral symptoms preceded ocular symptoms in 57% of these patients. Disease was limited to the eye in 22% of patients.

Although relatively rare, the incidence of ocular lymphoma has been increasing over the last 10 years, as more clinicians are considering this diagnosis in patients with chronic vitritis. Of the 42 patients with a definite diagnosis of ocular lymphoma, 69% were female. A female preponderance has also been described by Whitcup and associates.[126] The mean age of the patients with ocular lymphoma was 60.4 years (range, 35 to 82) in our series, which is slightly older than that of the patients of Whitcup and associates[126] (mean, 57.25 years; range, 37 to 75).

Many patients with possible ocular lymphoma are given a trial of systemic or periocular corticosteroids. If the uveitis totally resolves with steroid therapy, the patient is often given a presumptive diagnosis of idiopathic uveitis. Previous observers have suspected that in cases of ocular lymphoma

treated with corticosteroids, the inflammation will diminish, but low-grade inflammation may persist and recur when corticosteroids are tapered. The tumor may be sensitive to corticosteroids. Some investigators suggest that the use of corticosteroids prior to a diagnostic pars plana vitrectomy may reduce the sensitivity and specificity of the diagnostic procedure. Despite the use of preoperative corticosteroids, a diagnosis of intraocular lymphoma was cytologically made in 14 patients who received preoperative corticosteroids. A high degree of clinical suspicion remains important to diagnostic success. Chronic vitritis in middle-aged or older white patients, especially females, should be recognized as a characteristic of ocular lymphoma.

MISCELLANEOUS DISORDERS

Ten cases (34.5%) in the miscellaneous category had a diagnostic vitrectomy for epithelial ingrowth. The findings of some of these cases have been presented elsewhere.[127,128] Most cases (81%) were operated on between 1973 and 1984. However, as clinicians continue to explore newer surgical techniques for the management of different ocular diseases, one can expect epithelial ingrowth to present as a complication of some of these procedures,[129-131] the management of which can be difficult.[132]

The second group of cases within this category consists of patients who had a combined therapeutic and diagnostic pars plana vitrectomy for persistent hyperplastic primary vitreous. Some of these cases have been described previously,[133] as have patients with hemoglobin spherulosis[134] and amyloidosis.[135]

Other cytologic diagnoses made by diagnostic pars plana vitrectomy in this study included phacolytic reaction, phacoanaphylaxis,[136,137] lens-induced inflammation,[138] and asteroid hyalosis[139] (Table VIII).

The concurrent development of reliable cytopreparatory and surgical techniques has permitted analysis of vitreous samples obtained by pars plana vitrectomy. Much information has been gained about disease processes that involve the vitreous and adjacent ocular structures over the last 21 years.

With the advent of molecular biologic techniques,[140-142] which permit more specific and sensitive analysis of diseases that affect the vitreous, one can expect to learn more in the future about these diseases and how they can be brought under control by various surgical and medical therapeutic approaches.

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DISCUSSION

DR. MAURICE B. LANDERS III. Dr Palexas and associates present a report of 405 consecutive pars plana vitrectomies submitted to the eye pathology laboratory at the Wilmer Eye Institute, managed by Dr Green, for the 21-year period 1973 to1994. The paper also provides a review of the literature relating to many of the cases in this series.

This is a remarkable piece of work. The study deals with 405 diagnostic pars plana vitrectomies. These vitrectomies were performed by 134 different surgeons, with two thirds of the cases originating in the Wilmer Eye Institute and one third of the cases originating elsewhere.

There were relatively few cases submitted in the early years of the study; many more cases were submitted in the final years of the study. From 1973 through 1994, 85 cases were studied. From 1985 through 1994, 320 cases were studied. The authors suggest that this marked increase in the material submitted for evaluation was at least partially in response to a paper written by Dr Green and published in 1985 which describes the role of the eye pathology laboratory in the evaluation of diagnostic pars plana vitrectomies. I will return to this particular point shortly.

The study cases have been divided by the authors into six clinical groups: posttraumatic endophthalmitis, postoperative endophthalmitis, endogenous endophthalmitis, idiopathic inflammation, intraocular neoplasms, and miscellaneous.

There are innumerable "pearls" and pieces of valuable information throughout this study. Time permits the mention of only a few of them.

The authors point out that the diagnostic pars plana vitrectomy evaluation in the laboratory is a very good source of definitive information regarding endogenous infections. Of 24 cases submitted for suspected endogenous infections, microscopic organisms were identified in 21 of the 24 cases.

This study also points out the value of the eye pathology laboratory in the diagnosis of ocular lymphoma. Eighty seven cases of suspected ocular lymphoma were submitted in the course of this study. Forty two cases had a positive diagnosis, 42 cases had a negative diagnosis, and 3 cases were regarded as suspicious. The authors are also able to shed light on the effect of perioperative systemic corticosteroid use in the management of ocular lymphoma. Diagnostic pars plana vitrectomies were submitted in 14 cases suspected of ocular lymphoma in which perioperative steroids had been

used. The diagnosis was positive in all 14 cases, demonstrating that the use of perioperative steroids does not compromise this diagnostic procedure.

I would like to conclude my comments on this remarkable study with one question and one suggestion for the authors:

1. Would it be possible for Dr Green and his colleagues in the Wilmer Eye Pathology Laboratory, who have such extensive information in the area of diagnostic pars plana vitrectomies, to publish yet another paper on the subject? Perhaps they could provide explicit guidelines for those of us practicing vitreoretinal surgery regarding the interaction between the surgeon and the eye pathologist. Details of the specimen collection, communications with the eye pathology laboratory, fixation of the biopsy material, and shipment to the Wilmer Eye Pathology Laboratory, when indicated, would all be extremely helpful.
2. Keep up the good work.

I thank the authors for the opportunity to review and comment on this remarkable work.

DR. VINOD LAKHANPAL. This is an excellent paper by Dr Green and Dr Palexas. I have to share a very interesting case with you all and highlight some of the points that Dr Palexas has put forward. I had a very interesting patient in the last six months whom I have been following. He is a 70-year-old white male who was treated for chronic uveitis and vitritis for almost three years with topical and systemic steroids and non-steroidal anti-inflammatory agents elsewhere without any real significant effect. His vision was 20/25 and he was being followed by his ophthalmologist. The patient said that his vision is 20/25+ or 20/20 according to the ophthalmologist but "I have a smokey vision that is very annoying and very difficult to live with." Finally the patient was referred to me and I considered the possibility of ocular lymphoma. However, his fundus was totally negative for any retinal or choroidal lesions. A diagnostic vitrectomy, and a therapeutic vitrectomy at the same time, was done and here is the point that I would like to make. We sent those specimens to two hospitals but two different reports came out in reference to whether this case had lymphoma or not. This created further confusion in this patient. The patient had a significant past history of renal cell carcinoma and a prostate carcinoma which had been resected without any problems. Therefore, that made us more suspicious of a cancerous process going on in his body. This prompted us to do another vitrectomy in the other eye, and actually this was requested by the patient because he said that his vision after the first vitrectomy was so much better that he was not happy with his vision in the unoperated eye. He subsequently received a diagnostic and therapeutic vitrectomy in the second eye. So this time we made sure that the specimen went to the right place, and the right hands and at the right time. I therefore started a literature search and finally Dr Whitcup's[1] article came to my attention, and I think that is one of the best

articles that I have read on intraocular lymphoma. We sent the specimen as directed in the article to the NIH to Dr Solomon's attention. The authors had recommended that special culture medium (RPMI-1640) enriched with 10% fetal calf serum be used to send the specimen. In addition, they recommended that a very experienced cytopathologist review the slides immediately - a point which I wanted to make on my patient. The study came out positive for intraocular lymphoma, and I think this case is probably one of the most unique cases that I know because there is no retinal or choroidal lesion seen on fluorescein angiography. I think this might be the first case of this kind.

I would like to share two things. First of all, has anybody seen a case with only vitreous involvement without any retinal or choroidal involvement in ocular lymphoma? And number two question is, how do you treat this patient, ie, with chemotherapy and/or radiation, because so far, examination of all systems has proven negative for any lymphoma. In addition, spinal tap and MRI studies for CNS lymphoma have been negative. So basically the vitreous biopsy was the most important test towards the diagnosis of lymphoma in this patient.

Thank you.

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DR. JAMES J. AUGSBURGER. Because my interest is mostly with intraocular tumors, I will also comment on the portion of this paper pertaining to intraocular lymphoma. As many of you know, several of my colleagues and I presented a poster at the 1994 meeting of the American Academy of Ophthalmology concerning a series of 42 patients who underwent diagnostic posterior vitrectomy for suspected primary intraocular lymphoma at Wills Eye Hospital between 1986 and 1991. I would like to make several comments regarding our series of patients and then pose 3 questions for the authors.

First and foremost, only 12 of the 42 patients in whom our vitreoretinal surgeons suspected primary intraocular non-Hodgkins lymphoma had intravitreal lymphoma confirmed by cytopathologic study of the obtained specimen. Thus, lymphoma was confirmed by vitrectomy in about 29% of our cases as compared with about 50% of the series presented by Dr Palexas. One wonders why the percentage of cases with confirmed lymphoma is so much higher in the present series. I suspect that differences in inclusion criteria for the patients in the two series explain the observed difference in frequency of confirmed lymphoma.

Second, most ophthalmologists recognize that many patients who have

diffuse intravitreal cells as a prominent feature of their primary intraocular lymphoma eventually develop independent primary non-Hodgkin's lymphoma of the central nervous system (CNS). In our series of cases, 9 of the 12 patients with cytologically confirmed intravitreal lymphoma either had or developed CNS lymphoma during followup. However, two of our patients developed visceral soft tissue lymphoma but not CNS lymphoma during their followup. It is important for clinicians to recognize that visceral non-Hodgkin's lymphoma is occasionally associated with primary intraocular lymphoma that manifests itself with prominent intravitreal cells.

Third , in our series of cases, none of the 30 patients who were diagnosed as having a nonlymphoma disorder on the basis of their initial vitrectomy developed lymphoma in the CNS or visceral soft tissues during followup or was confirmed to have intraocular lymphoma on a subsequent ocular biopsy. One wonders if any of the patients in the present study who were felt to have a nonlymphoma disorder initially were subsequently confirmed to have lymphoma.

My questions for the authors are as follows: (1) How do you account for the substantially higher percentage of cytologically confirmed lymphoma in your series than in ours? (2) Did any of the patients in your series who were diagnosed as having a nonlymphoma disorder on the basis of their diagnostic vitrectomy subsequently develop either CNS or visceral lymphoma? (3) How many of your patients with intravitreal lymphoma confirmed by cytopathologic study of the initial vitreous specimen subsequently developed visceral soft tissue lymphoma, CNS lymphoma, or both?

DR. RICHARD FORSTER. I enjoyed this paper very much, and wish to ask the authors a few questions. Even though I think the data has been looked at carefully, and was beautifully presented this morning, I would like to ask how the data was collected, interpreted, and what criteria were utilized. There are basically three ways that have evolved to sample the vitreous in cases of endophthalmitis. Beginning in the early 1970s, tapping of the vitreous and aspirating liquid contents was later enhanced by a vitreous biopsy technique popularized by Dr. Doft, consisting of a diagnostic sample obtained with a vitreous instrument through the pars plana. And beginning about 1976, sampling of the vitreous was performed at the time of therapeutic pars plana vitrectomy. So, I would like to ask the authors first of all if they have an indication as to what technique was used to sample the vitreous?

Secondly, surprising to me is the observation that only about 17% of postoperative trauma and bleb-related endophthalmitis were positive by culture, and yet approximately 27% were considered diagnostic by histopathologic microscopy. That is the opposite of what I would expect when looking at samples under the microscope compared to culture; that is, the culture has been considered the gold standard to identify infection, and

we have accepted the fact that we are not going to find as many organisms in a vitreous sample examined microscopically as we would detect on culture growth. So I would like to ask specifically, what criteria were used for the microscopic diagnosis of an intraocular infection? In addition, I also would like to ask what microbiologic criteria were used to identify a positive culture in a case of presumed infectious endophthalmitis?

DR. ROBERT RITCH. I would like to congratulate the authors on the highly informative paper and I have one question.

I noticed that your postoperative endophthalmitis glaucoma cases were clustered in 1994. This date coincides with a major shift from the use of 5-Fluorouracil to Mytomicin-C. Were these endophthalmitis cases related to the use of Mitomycin-C?

DR. THOMAS P. KEARNS. Some of the senior members in attendance today will recall that Dr Verhoeff would often discuss a paper by pointing out that the author forgot to mention his reference on the subject. I do not want to mimic Dr Verhoeff but I do want to point out an early reference of mine on intraocular lymphoma. Dr Green, you are aware of the fact that some of the earlier reports of this subject were from the Mayo Clinic but I do not believe that you are aware that I presented a paper on this subject at one of the neuro-ophthalmology meetings at the Wilmer Institute in 1969 (Van Scoy RE, Kearns TP, MacCarty CS, Hill RW: Uveitis and Reticulum Cell Sarcoma of the Brain - Abstract, Excerpta Medica International Congress Series 1969; 193:84-85). Although we incorrectly assumed that the intraocular component was a uveitis I believe that this was the earliest reference of this interesting and important association.

DR. GEORGE PALEXAS. Thank you Dr Spivey. First I would like to thank Dr Landers for his comments and discussion. Details on how specimen collection should be carried out, fixation of the biopsy material and shipment to the Wilmer Eye Pathology Laboratory for histopathological analysis should be discussed with Dr Green, before a diagnostic vitrectomy is performed and submitted to the laboratory. Dr Green will on consultation provide each clinician with the necessary guidelines on how the vitrectomy specimens should be managed, as proper preservation of the biopsy material is critical.

I would like to thank Dr Lakhanpal for sharing his interesting case of a 67-year-old white male with us. The patient had a two to three year history of chronic vitritis, which was unresponsive to steroids, and required multiple diagnostic vitrectomies before a diagnosis of ocular lymphoma was made. The question of what is the best therapy for patients with ocular lymphoma is presently unknown. There is an ongoing prospective study at the National Institutes of Health, in which patients who present with ocular lymphoma are being randomized to radiotherapy, chemotherapy or to both treatment

modalities. These studies will hopefully provide us with some insight on how best to manage patients who present with ocular lymphoma.

Dr Augsburger questioned the high percentage of cases (48%) 42 out of 87 patients, who were suspected of ocular lymphoma in the surgeons pre-vitrectomy differential diagnosis and subsequently confirmed histologically at the Wilmer Eye Pathology Laboratory. This percentage of 48 is higher than the percentage af 29, 12 or 42 cases which were studied between 1986 and 1991 by Dr Augsburger in his series at the Wills Eye Hospital. I would like to point out that the cases referred to Dr Green at the Wilmer Institute are cases that came from a selected group of patients, both from the Wilmer Institute and from elsewhere. Many of these patients presented with a problem of diagnosis clinically, often with chronic vitritis and not responding to steroids, some of which had repeat diagnostic vitrectomies elsewhere with no definitive diagnosis, until a specimen was referred to Dr Green for an opinion. This may in part reflect the higher percentage of positive patients given as a 48% from our study compared to Dr Augsburger's figure of 29%. The question of how many of the 42 patients who had vitreous involvement went onto develop extraocular lymphoma is a question that I am afraid I cannot give you an exact answer to. In a series of 32 patients published by Freeman LN et al, in *Opthalmology* in 1987, the surgical cases of which are included in this study, CNS involvement occurred in 56% (18 of 32) cases, and in these patients the ocular symptoms preceded CNS symptoms. Visceral involvement occurred in 16% of patients, and occurred with CNS disease in 6%. The disease was limited to the eye in 22% of patients.

Dr Forster wanted to know whether the vitreous samples which were obtained from the 215 cases with suspected infectious endophthalmitis were obtained by vitreous tap, aspiration or vitreous biopsy. In this study we excluded all patients that had a vitreous tap. Only those cases which were coded as having a diagnostic vitrectomy or aspiration were included in this series. The second question which Dr Forster asked was, on what basis was a case classified and confirmed as infected. This was based on microscopical features and was based on identifying organisms by gram stain, or other special stains that allow for microscopical identification of organisms in vitreal samples. In cases which had viruses these infections were confirmed by electron microscopy. The microbiological diagnosis was established by growing the same organism, on two different culture media, from the same vitreous sample. These reports were obtained from the microbiology laboratories. Dr Forster was surprised to see that in our series the number of infected cases which were culture-proven were fewer than the microscopically-proven cases, a difference of 8.1%. The differences seen may in part be to the viability of organisms and culture techniques.

Dr Ritch wanted to know whether cases which had filtering procedures in the early 1990's and which later presented with bleb related postoperative endophthalmitis, if these had adjunctive antimetabolite therapy at the

time of surgery. Three out of the 11 cases with post operative bleb related endophthalmitis did have a history of antimetabolite use, all three of which were operated in the early 1990's.

Thank you.