Chapter 38
Diagnostic Vitrectomy and the Cancer Patient: Special Considerations

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Abstract The term *diagnostic vitrectomy* is used to refer to biopsy of the vitreous or the uvea. In patients with a history of cancer, there is a low clinical threshold for diagnostic vitrectomy as vitritis can represent recurrence of lymphoma or leukemia or an opportunistic infection. The most common clinical scenarios in which diagnostic vitrectomy is performed in cancer patients are new-onset vitreous cellularity in a patient with lymphoma in remission or newly diagnosed lymphoma; vitritis in a patient with recent bone marrow transplantation; atypical retinitis or choroiditis; and atypical iris, ciliary body, or choroidal lesions. In addition, choroidal biopsy is sometimes done to obtain material for cytogenetic studies in patients with uveal melanoma. Vitreous biopsy can be performed successfully with either a two-port or three-port approach; specifics of the technique depend on the vitrector gauge. Uveal biopsy can be performed with fine-needle aspiration biopsy or with transretinal choroidal biopsy with a sutureless vitrectomy system, an approach that is gaining favor. Collaboration and good communication between the ophthalmologist and a pathologist well versed in the handling and analysis of vitreous samples are essential for successful diagnostic vitrectomy.

38.1 Introduction

Diagnostic vitrectomy in cancer patients is used in a wide range of clinical scenarios (Fig. 38.1). Patients with a history of cancer may experience decreased vision or other visual symptoms associated with vitreous hemorrhage, vitritis, retinitis, and/or chorioretinitis. These presentations pose diagnostic challenges, as they can signify a primary intraocular, primary extraocular, or metastatic malignancy; the recurrence of a malignancy; and even a paraneoplastic syndrome or conditions unrelated to

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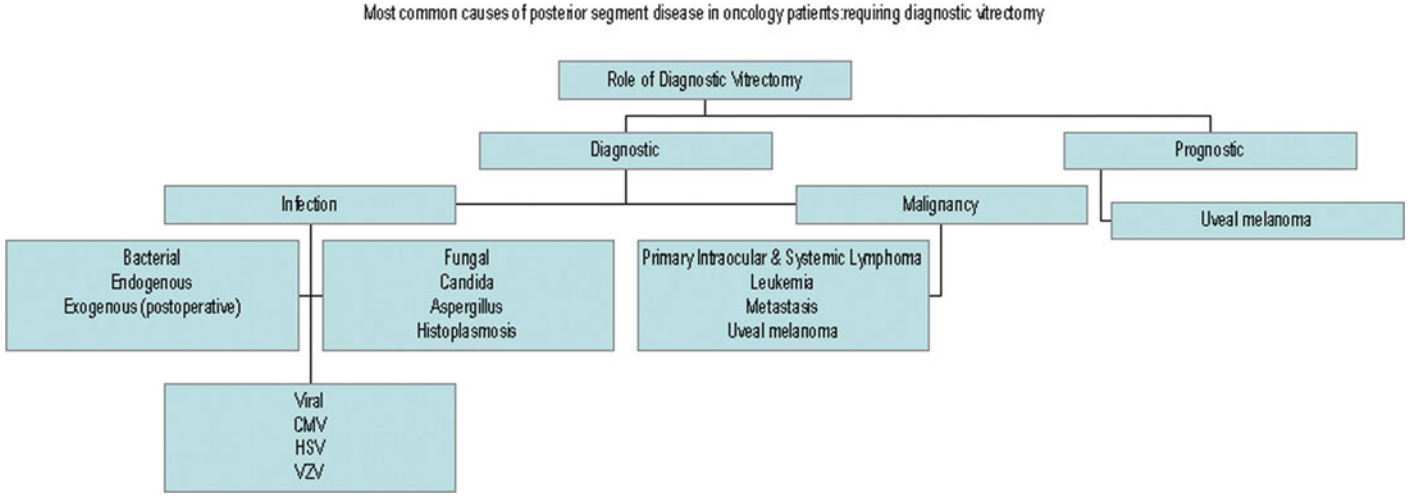

Fig. 38.1 Most common causes of posterior segment disease in cancer patients requiring diagnostic vitrectomy. CMV, cytomegalovirus; HSV, herpes simplex virus; HZV, herpes zoster virus

malignancy [1–3]. The diagnostic challenge is further complicated by iatrogenic immunosuppression from oncologic treatment, which can result in opportunistic fungal, bacterial, and/or viral infections [4–6]. Patients with a history of hematopoietic malignancy in remission may have autoimmune conditions associated with ocular inflammation, such as sarcoidosis or systemic lupus erythematosus.

Often, the etiology of vitreous cells can be determined by careful patient history and clinical examination; however, a tissue diagnosis obtained through vitrectomy is very helpful in many instances. Diagnostic vitrectomy and pathologic analysis of the vitrectomy specimen are well-accepted procedures for the confirmation or exclusion of ocular disorders [7–10].

38.2 Indications for Diagnostic Vitrectomy

The term *diagnostic vitrectomy* is used to refer to biopsy of either of two separate ocular entities, the vitreous and the uvea.

Uncomplicated diagnostic vitrectomy is a low-risk procedure providing valuable clinical benefits. The most common clinical scenarios are new-onset vitreous cellularity in a patient with lymphoma in remission or newly diagnosed lymphoma; vitritis in a patient with recent bone marrow transplantation; atypical retinitis or choroiditis; and atypical iris, ciliary body, or choroidal lesions.

38.2.1 Vitreous Biopsy

The most common indications for vitreous biopsy in cancer patients are vitreous cells or opacities of uncertain nature and vitreous hemorrhage of unknown etiology. In patients with a history of cancer, there is a low clinical threshold for vitrectomy as vitritis can represent recurrence of lymphoma or leukemia or an opportunistic infection. Vitreous hemorrhage can obscure the diagnosis of an ocular neoplasm [11].

38.2.2 Uveal Biopsy

Many tumor types arise in the choroid, each with a variety of clinical manifestations. In almost all patients, a choroidal tumor can be diagnosed readily by performing binocular indirect ophthalmoscopy. Ancillary tests such as echography and angiography can provide confirmatory evidence in some patients. In some instances, it is difficult to establish the diagnosis especially in cases of atypical melanoma or other choroidal lesions, choroidal metastasis, and rare lesions like retinal pigmentary adenoma and neurolemmoma.

Another emerging indication for choroidal biopsy is cytogenetic studies in patients with uveal melanoma. Uveal melanoma is the most common primary cancer of the eye. It often results in vision loss, and in up to half of patients, it results in death due to metastases. For many years, the details of the molecular pathogenesis of uveal melanoma remained elusive. In the past decade, however, many of these details have emerged to reveal a fascinating and complex story of how the primary tumor evolves and progresses. Early events that disrupt cell cycle and apoptotic control lead to malignant transformation and proliferation of uveal melanocytes. Later, the growing tumor encounters a critical bifurcation point, where it progresses along one of two genetic pathways with very distinct genetic signatures (monosomy 3 vs 6p gain) and metastatic propensity. Late genetic events are characterized by increasing aneuploidy, most of which is nonspecific. However, specific chromosomal alterations, such as loss of chromosome 8p, can hasten the onset of metastasis in susceptible tumors. This pathogenetic scheme can be used to construct a molecularly based and prognostically relevant classification of uveal melanomas for personalized patient management, particularly in the setting of metastatic disease [12].

It ought to be noted that biopsy using vitrector instrumentation is being increasingly employed for uveal biopsies.

38.3 Preoperative Considerations

Preoperative considerations in cancer patients scheduled to undergo vitrectomy are similar to those in noncancer patients. Patients should undergo a thorough ocular examination and a general examination to assess anesthetic risk. Cancer patients may be ill and must be stable enough to undergo moderate sedation. Although diagnostic vitrectomy is usually performed with retrobulbar or sub-Tenon injection of local anesthesia and monitored sedation, most anesthesiologists prefer that the patient be medically stable enough for general anesthesia [13]. Most elderly patients require baseline electrocardiography. As cancer patients may have blood cell count abnormalities, e.g., pancytopenia, a complete blood cell count is essential to determine whether transfusions or other precautions may be warranted. Other laboratory tests may be indicated depending on the clinical situation.

38.3.1 Thrombocytopenia

Ocular manifestations of thrombocytopenia include retinal and vitreal hemorrhage, retinal detachment, papilledema, and disc neovascularization. There are no published reports with which to define a minimum safe platelet count for vitrectomy in patients with thrombocytopenia. One study of 11 thrombocytopenic patients undergoing cataract and glaucoma surgery showed that the incidence of hemorrhagic complications was 18% [14]. We generally follow the recommendations of the

consensus panel of the British Committee for Standards in Hematology and prefer to have a platelet count above 70,000 per mm^3 of blood (normal is 150,000–400,000 per mm^3 of blood) [15]. In cases of severe thrombocytopenia, frozen platelet transfusion 1–2 hours before surgery is arranged after consulting with a hematologist [15].

38.3.2 Anesthesia

Local anesthesia is commonly obtained with a mixture of bupivacaine (5 mg/ml), lidocaine (10 mg/ml), and hyaluronidase using a retrobulbar, peribulbar, or sub-Tenon insertion technique [16–18]. The block is placed while the patient is under conscious sedation. Recent studies of patients undergoing unilateral ophthalmic surgery with retrobulbar or peribulbar anesthesia showed no difference in patient satisfaction or clinical success between patients who did and those who did not have intravenous sedation [19, 20]. However, given that some cancer patients are critically ill and may have positional discomfort, operative efficiency and patient satisfaction in cancer patients are often enhanced with the use of intravenous sedation. Effective communication and good relationships between the ophthalmologists and the anesthesiologists facilitate excellent patient care.

Despite reports of complications with retrobulbar technique, it is generally accepted that the risk of retrobulbar hemorrhage is low. However, sub-Tenon's anesthetic insertion is occasionally employed, particularly in patients with abnormally functioning platelets or platelet counts below 50×10^9/l. There have been only two published reports of retrobulbar hemorrhage following sub-Tenon's block [19].

38.4 Vitreous Biopsy

38.4.1 Technique

Both two-port and three-port approaches have been successfully employed to obtain vitreous samples. We favor a three-port approach under noncontact wide-angle stereoscopic viewing because of the control and safety that this approach affords the surgeon (Fig. 38.2). There are currently three vitrector gauges available (20, 23, and 25), and all three are used by our surgeons.

Specifics of the technique vary depending on the vitrector gauge. After the patient has been anesthetized and sterile technique applied, an infusion cannula is inserted through the pars plana inferotemporally. Proper cannula placement is confirmed visually, but in order to preserve an undiluted sample, irrigation is not initiated. A second vitrectomy port is created superonasally and is temporarily occluded with a vitrectomy port plug to prevent vitreous prolapse during placement of the final port. A third vitrectomy port is created superotemporally. Instruments in the vitreous cavity are visualized using a binocular indirect ophthalmomicroscope (BIOM). With

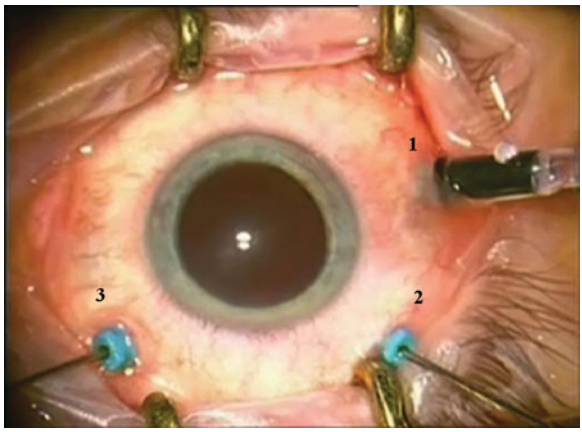

Fig. 38.2 Sutureless 25-G vitrectomy showing (1) infusion, (2) vitrector, and (3) endoilluminator

the infusion occluded, the assistant slowly aspirates undiluted vitreous (through a 3-cc syringe connected to the vacuum tubing from the vitrector) while the surgeon activates the cutter. As the surgeon guides the cutter toward the areas with the densest vitritis, 1.0–1.5 ml of vitreous is collected in the syringe and the eye begins to deflate. The assistant stops aspirating, and the surgeon removes the vitrectomy handpiece from the eye. The assistant can then collect an additional 0.5 ml of undiluted vitreous from the dead space in the tubing into the syringe, which is immediately capped and labeled. The vitreous cavity is then infused with balanced salt solution. If clinically appropriate, an additional core vitrectomy is performed and diluted vitreous in the cassette is sent for cytologic examination. After peripheral examination confirms the absence of peripheral retinal tears, the instrumentation is removed, and the sclerotomy sites either self-seal or are closed with Vicryl sutures.

The amount of undiluted vitreous acquired is limited by hypotony and the risk of suprachoroidal hemorrhage. The risk of suprachoroidal hemorrhage can be minimized by having the assistant perform simultaneous scleral indentation (Fig. 38.3). This maneuver helps to avoid hypotonous complications by stabilizing the intravitreal pressure in the absence of irrigation fluid. Utilizing this technique, we have not encountered any complications in more than 100 vitreous and choroidal biopsies.

Some authors have described a perfluorocarbon-perfused vitrectomy technique that allows an average of 2.24 ml of undiluted vitreous to be removed [21–24]. A syringe of perfluorocarbon liquid is connected to the infusion line. Vitreous is aspirated as the perfluorocarbon is infused. The difference in densities allows separation of the fluids during vitrectomy and processing. However, we do not routinely employ this technique because repeated fluid exchanges add significant complexity to the procedure. The undiluted vitreous is sent to the laboratory for cytologic evaluation, antibody determinations, and polymerase chain reaction (PCR) amplification. The diluted vitreous specimen from the syringe and the vitrectomy cassette can be evaluated with flow cytometry and with bacterial, fungal, and viral cultures.

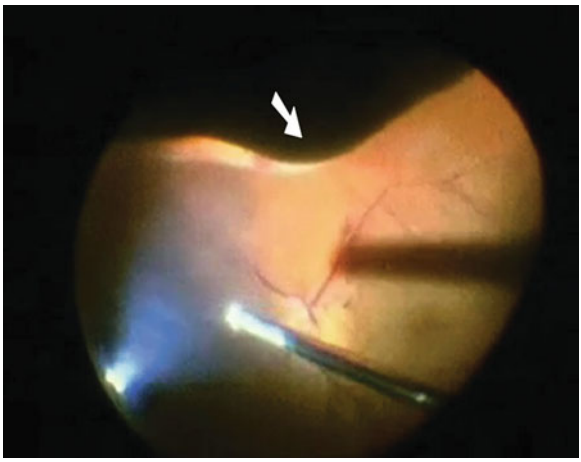

Fig. 38.3 Vitreous biopsy; note scleral indentation (*arrow*) to stabilize intravitreal pressure during dry vitreous sample retrieval

38.4.2 Effect of Vitrector Gauge on Vitreous Sample

Experimental models have shown that obtaining samples by vitrectomy causes minimal damage to human cell structure and should not limit cytologic assessment [25]. Conlon et al. [26] found that suspensions of human leukemic cells that were aspirated through a vitrector could not be distinguished from control cells on cytologic assessment. Vitrectomy had no observable effect on cell preservation using membrane filtration or cytocentrifugation techniques. Various aspiration and guillotine vitrector cutter rates even up to 1500 cuts per minute neither alter the yield of bacterial specimens nor affect the clinical utility of vitreous samples [27]. Higher cut rates mildly reduce the fungal yield and significantly reduce leukocyte viability.

The 25- and 23-G instruments minimize surgically induced trauma from sclerotomy sites, allow for self-sealing (sutureless) sclerotomies, improve operative efficiency, and hasten postoperative recovery. The absence of sutures prevents suture-based complications such as suture irritation, scleral pigmentary changes, and astigmatism induced by tight scleral sutures [28].

38.5 Uveal Biopsy

38.5.1 Technique

Fine-needle aspiration biopsy (FNAB) has traditionally been used for uveal biopsies. For preequatorial tumors, FNAB involves a transscleral approach and a 30-G needle; for postequatorial tumors, FNAB involves a transvitreal approach and a 27-G needle [29]. However, FNAB yields insufficient samples for cytogenetic analysis, and given the recently emphasized importance of cytogenetic testing, transretinal choroidal biopsy (TRCB) with sutureless vitrectomy systems is gaining favor.

TRCB involves insertion of 25-G infusion port, light pipe, and vitreous cutter cannulae 4 mm from the limbus in phakic eyes and 3.5 mm from the limbus in pseudophakic eyes. To separate the conjunctival and scleral openings, the conjunctiva is mobilized toward the corneal limbus with non-toothed forceps as the port is inserted. If a radioactive plaque is inserted during the same operation, the tumor biopsy is performed after these procedures are completed, with the ports passed through undisturbed conjunctiva. The vitreous cutter is advanced across the vitreous cavity and through the retina into the center of the tumor. Tissue samples are taken by rotating the cutter within the tumor. The vitreous cutter is repeatedly withdrawn from the tumor and flushed with a small volume of vitreous to prevent blockage of the aspiration cannula by tumor fragments. A complete vitrectomy is not performed. The specimen is back-flushed into a sterile specimen bottle through the cutter. Tumor fragments are visualized in the specimen bottle under the operating microscope to confirm that an adequate sample has been obtained.

When the scleral ports are removed, cotton-tipped applicators are used to apply pressure to each entry site and stroke the conjunctiva back into position. The aspirate is placed in a sterile container with an equal volume of 10% neutral buffered formalin. This preparation is then centrifuged. The resulting pellet is embedded in agar, and the preparation is processed into paraffin wax. Sections of the resulting wax-embedded cell block are stained with hematoxylin–eosin or periodic acid-Schiff or with immunohistochemical methods.

38.5.2 Complications

One of the authors (GK) observed vitreous hemorrhage in 32 (23%) of 140 cases (personal experience). In most of the patients, vitreous hemorrhage resolved spontaneously over 3–4 weeks, but 25% of affected patients needed vitrectomy to clear the vitreous hemorrhage.

No other intraoperative or postoperative complications were encountered. There are concerns about tumor recurrence or spread after uveal biopsy due to intraocular or extraocular seeding of tumor cells. However, the authors' experience with primary transretinal resection of 60 uveal melanomas over a 5-year period indicates that tumor recurrence from any seeding is rare [30]. The scleral cannula used with the 25-G system should further reduce any chances of implanting tumor cells into the entry sites.

38.5.3 Collaboration with Pathology

Collaboration with a skilled pathologist is essential to successful diagnostic vitrectomy. After a surgical date and time have been set, a pathologist experienced in

the analysis of vitreous samples should be contacted and informed of the approximate arrival time of the sample. The likely diagnoses should be discussed with the pathologist, and the pathologist's preference for sample handling should be followed. Lymphoma cells degrade quickly, and some authors recommend placing the sample into a tube containing Roswell Park Memorial Institute culture medium [31]. Placement of the sample into normal saline can be helpful; however, alcohol fixation is not recommended because this can jeopardize identification of lymphoma cells.

We routinely place samples on ice and transport them directly to the laboratory after collection. We prefer immediate processing; samples are not stored overnight.

38.6 Pathologic Processing

There are three classes of laboratory testing for vitreous samples: (1) direct detection of the pathogen, which can be accomplished using cytology, staining and microscopic analysis, and cultures for fungi, bacteria, or viruses; (2) detection of the host response, which is accomplished by measuring interleukin; and (3) indirect detection of the pathogen, which is accomplished by using PCR. The most commonly used techniques at our institution are cytology, microscopic analysis, cultures, and PCR.

38.6.1 Cytology

Cytologic analysis of the vitreous sample is the primary technique for diagnosis of malignancy; however, necrotic cells, debris, and reactive inflammatory cells can pose a diagnostic challenge [32]. When intraocular lymphoma is suspected, characteristic features can be revealed using Giemsa, Papanicolaou, or Diff-Quick staining. A normal population of inflammatory cells would suggest infection or nonmalignant uveitis [33].

Flow cytometry can prove a useful supplement in the diagnosis of primary intraocular lymphoma [34]. Most primary intraocular lymphomas are monoclonal populations of B lymphocytes, and flow cytometry can simultaneously assess several different markers to confirm monoclonality in primary intraocular lymphoma.

38.6.2 Interleukin Measurement

Interleukin-10, a lymphoma cell growth factor, has been found to be elevated in vitreous samples of patients with intraocular lymphoma [35, 36]. Chan et al. [35] analyzed concentrations of five different interleukins (1, 2, 4, 6, and 10) by enzyme-linked immunosorbent assay in vitrectomy specimens from three patients with

primary intraocular lymphoma and five patients with uveitis. Interleukin-10 was detected in the patients with lymphoma, and its levels correlated with clinical activity. Other studies have shown that elevated interleukin levels, although helpful, are not always associated with intraocular or central nervous system lymphoma [37]. The specificity of this test is still in doubt, and further studies are needed to ascertain its utility.

38.6.3 Polymerase Chain Reaction

PCR is a technique used to amplify small amounts of genetic material for analysis. The utility of PCR in vitrectomy samples may be particularly great in patients suspected of having infectious endogenous endophthalmitis. In such situations, short sequences of pathogen DNA are combined with the vitreous sample. If the vitreous sample contains matching strands of DNA, the pathogen DNA molecule acts as a primer, allowing the enzyme DNA polymerase to replicate the DNA. PCR has been used to detect many different bacterial, fungal, parasitic, and viral ocular infections. PCR is most commonly used at our institution to detect cytomegalovirus, herpes simplex virus, varicella zoster virus, and *Toxoplasma gondii*. PCR is readily available but may require collaboration with an outside laboratory.

38.6.4 Genetic Analysis

Intraocular lymphoma is often diagnosed by visualization of atypical cells or by flow cytometry. Genetic analysis may be important for determining clinical prognosis. Wallace et al. performed genetic analysis on the vitreous samples of 72 patients with primary intraocular lymphoma [38]. The authors evaluated the presence of the *bcl-2* t(14;18) translocation, the *bcl-10* gene, and the expression of *bcl-6* mRNA in primary intraocular lymphoma cells. The authors attempted to correlate the presence of the *bcl-2* t(14;18) translocation with clinical prognosis.

Although the authors could not correlate the presence of *bc1-2* t(14;18) with clinical prognosis, primary intraocular lymphoma was found to have unique molecular patterns of *bcl-2*, *bcl-10*, and *bcl-6* compared with other systemic lymphomas. This study may lay the foundation for future studies using gene expression profiling to supplement pathologic diagnosis of complex diseases.

38.6.5 Cytogenetic Uveal Melanoma Studies

The details of cytogenetic analysis techniques for uveal melanoma are beyond the scope of this chapter. However, commonly used techniques are fluorescence in situ hybridization (FISH), comparative genomic hybridization, and, most recently,

multiplex ligation-dependent probe amplification (MLPA), which is reliable and cost-effective [39].

38.7 Results of Diagnostic Vitrectomy

38.7.1 Common Diagnoses

The clinical utility of diagnostic vitrectomy depends on the nature of the case. The largest series of diagnostic pars plana vitrectomy was published by Palexas et al. [40], who conducted a retrospective study covering 21 years. Pathology samples from 405 consecutive patients at the Wilmer Eye Institute revealed that the breakdown of results was as follows: posttraumatic infections, 8.4%; postoperative endophthalmitis, 38.5%; endogenous endophthalmitis, 6.2%; idiopathic inflammation, 25.4%; intraocular neoplasm, 14.3%; and miscellaneous, 7.2%. Palexas et al. [40] found that when the clinician suspected ocular lymphoma, 42 of 87 patients (48%) had positive biopsies. When the clinician suspected endogenous endophthalmitis, 23 of 25 biopsies (92%) were positive.

38.7.2 Diagnostic Utility

The vast majority of vitreous biopsies performed at The University of Texas M. D. Anderson Cancer Center are done to confirm or exclude intraocular malignancy or infection.

Davis et al. [9] reviewed cases to assess the utility of diagnostic tests performed on vitrectomy specimens from patients with suspected lymphoma or infection. Seventy-eight consecutive patients (84 eyes) underwent pars plana vitrectomy with cytologic, cytofluorographic, or microbiologic analysis. There were 33 eyes (28 patients) with suspected intraocular lymphoma and 51 eyes (50 patients) with suspected infection. Diagnostic vitrectomy led to the diagnosis in 48 of the 78 patients (61.5%). The biopsies for 14 patients were positive for lymphoma or leukemia and for 34 patients were positive for infection.

In this study, diagnostic vitrectomy for two of the most common indications at M. D. Anderson, lymphoma and infection, revealed a positive predictive value of 100%, and negative predictive values of 70 and 95%, respectively [9].

In contrast to the 70% negative predictive value for lymphoma reported by Davis et al. [9], a 98% negative predictive value was reported by Zhai et al. [41]. These authors reviewed the clinical records of 54 patients whose vitreous fluid samples were reported as “negative for malignancy” by an experienced pathologist. The main indication for vitrectomy was confirmation of intraocular inflammation. There was only 1 false-negative case identified among 54 cytologically benign

vitreous samples. The negative predictive value of diagnostic vitrectomy in this study was 98%.

38.8 Postoperative Considerations

Patients are prescribed a combination of a topical steroid and an antibiotic to be taken for 2–3 weeks following diagnostic vitrectomy. Patients are understandably concerned about the results of the procedure and should have the results communicated as soon as possible. Verbal communication with the cytopathologist confirming the presence or absence of malignant cells on cytology is expected promptly, and the patient is usually notified of the preliminary results on the first postoperative visit. Usually the cytology result is available within 24 hours. Final results from PCR and fungal, bacterial, and/or viral cultures often require a week.

Postoperative complications include cataract, glaucoma, hypotony, infection, and retinal tear or detachment. Fortunately, the complication rate following vitrectomy is low. Palexas et al. and Scott et al. reported an overall incidence of endophthalmitis of 0.03% for 20-G vitrectomy and 0.84% for 25-G vitrectomy [40, 42].

38.9 Conclusion

Diagnostic vitrectomy in a patient with a known or suspected history of cancer is a useful tool in the diagnosis and management of ocular inflammation of unknown etiology. Generally, a low threshold for biopsy is required in patients with a history of cancer. Collaboration and good communication between the ophthalmologist and a pathologist well versed in the handling and analysis of vitreous samples are essential.

References

1. Robertson DM, Wilkinson CP, Murray JL, et al. Metastatic tumor to the retina and vitreous cavity from primary melanoma of the skin: treatment with systemic and subconjunctival chemotherapy. Ophthalmology 1981;88(12):1296–1301.
2. Jaissle GB, Szurman P, Rohrbach JM, et al. A case of cutaneous melanoma metastatic to the vitreous cavity: possible pathomechanism and review of the literature. Graefes Arch Clin Exp Ophthalmol 2007;245(5):733–40.
3. Soheilian M, Mirbabai F, Shahsavari M, et al. Metastatic cutaneous melanoma to the vitreous cavity masquerading as intermediate uveitis. Eur J Ophthalmol 2002;12(4):324–7.
4. Greene WH, Wiernik PH. Candida endophthalmitis. Successful treatment in a patient with acute leukemia. Am J Ophthalmol 1972;74(6):1100–4.
5. Rogers SJ, Johnson BL. Endogenous Nocardia endophthalmitis: report of a case in a patient treated for lymphocytic lymphoma. Ann Ophthalmol 1977;9(9):1123–31.
6. Lamaris GA, Esmaeli B, Chamilos G, et al. Fungal endophthalmitis in a tertiary care cancer center: a review of 23 cases. Eur J Clin Microbiol Infect Dis 2008;27(5):343–7.
7. Engel HM, Green WR, Michels RG, et al. Diagnostic vitrectomy. Retina 1981;1(2):121–49.

8. Green WR. Diagnostic cytopathology of ocular fluid specimens. Ophthalmology 1984;91(6):726–49.
9. Davis JL, Miller DM, Ruiz P. Diagnostic testing of vitrectomy specimens. Am J Ophthalmol 2005;140(5):822–9.
10. Foulds WS. The uses and limitations of intraocular biopsy. Eye 1992;6(Pt 1):11–27.
11. Saro F, Clua A, Esteva E, et al. Cytologic diagnosis of ocular melanocytoma: a case report. Acta Cytol 2008;52(1):87–90.
12. Landreville S, Agapova OA, Harbour JW. Emerging insights into the molecular pathogenesis of uveal melanoma. Future Oncol 2008;4:629–36.
13. Rosenfeld SI, Litinsky SM, Snyder DA, et al. Effectiveness of monitored anesthesia care in cataract surgery. Ophthalmology 1999;106(7):1256–60; discussion 1261.
14. Papamatheakis DG, Demers P, Vachon A, et al. Thrombocytopenia and the risks of intraocular surgery. Ophthalmic Surg Lasers Imaging 2005;36(2):103–7.
15. Saeed MU, Wong D, Heimann H, et al. Spontaneous progressive supra-choroidal haemorrhage in a patient undergoing haemodialysis. Graefes Arch Clin Exp Ophthalmol 2007;245(11):1741–2.
16. Hamilton RC. Retrobulbar block revisited and revised. J Cataract Refract Surg 1996;22(9):1147–50.
17. Duker JS. Retrobulbar injections: standards of care. Surv Ophthalmol 1995;39(4):344–5.
18. Demediuk OM, Dhaliwal RS, Papworth DP, et al. A comparison of peribulbar and retrobulbar anesthesia for vitreoretinal surgical procedures. Arch Ophthalmol 1995;113(7):908–13.
19. Kallio H, Uusitalo RJ, Maunuksela EL. Topical anesthesia with or without propofol sedation versus retrobulbar/peribulbar anesthesia for cataract extraction: prospective randomized trial. J Cataract Refract Surg 2001;27(9):1372–9.
20. Lim TH, Humayun MS, Yoon YH, et al. The efficacy of retrobulbar block anesthesia only in pars plana vitrectomy and transconjunctival sutureless vitrectomy. Ophthalmic Surg Lasers Imaging 2008;39(3):191–5.
21. Quiroz-Mercado H, Garcia-Aguirre G, Ustariz-Gonzalez O, et al. Perfluorocarbon-perfused vitrectomy using a transconjunctival 25-gauge system. Retina 2007;27(7):926–31.
22. Quiroz-Mercado H, Rivera-Sempertegui J, Macky TA, et al. Performing vitreous biopsy by perfluorocarbon-perfused vitrectomy. Am J Ophthalmol 2005;140(6):1161–3.
23. Quiroz-Mercado H, Guerrero-Naranjo J, Agurto-Rivera R, et al. Perfluorocarbon-perfused vitrectomy: a new method for vitrectomy—a safety and feasibility study. Graefes Arch Clin Exp Ophthalmol 2005;243(6):551–62.
24. Quiroz-Mercado H, Suarez-Tata L, Magdalenic R, et al. Perfluorocarbon perfused vitrectomy: animal studies. Am J Ophthalmol 2004;137(2):287–93.
25. Huang JS, Russack V, Flores-Aguilar M, et al. Evaluation of cytologic specimens obtained during experimental vitreous biopsy. Retina 1993;13(2):160–5.
26. Conlon MR, Craig I, Harris JF, et al. Effect of vitrectomy and cytopreparatory techniques on cell survival and preservation. Can J Ophthalmol 1992;27(4):168–71.
27. Ratanapojnard T, Roy CR, Gariano RF. Effect of vitrector cutting rate on vitreous biopsy yield. Retina 2005;25(6):795–7.
28. Van Kuijk FJ, Uwaydatt S, Godley BF. Self-sealing sclerotomies in pars plana vitrectomy. Retina 2001;21:547–50.
29. Shields CL, Ganguly A, Materin MA, et al. Chromosome 3 analysis of uveal melanoma using fine-needle aspiration biopsy at the time of plaque radiotherapy in 140 consecutive cases. Trans Am Ophthalmol Soc 2007;105:43–53.
30. Damato B, Groenewald C, McGalliard J, et al. Endoresection of choroidal melanoma. Br J Ophthalmol 1998;82:213–8.
31. Whitcup SM, Chan CC, Buggage RR, et al. Improving the diagnostic yield of vitrectomy for intraocular lymphoma. Arch Ophthalmol 2000;118(3):446.
32. Margolis R. Diagnostic vitrectomy for the diagnosis and management of posterior uveitis of unknown etiology. Curr Opin Ophthalmol 2008;19(3):218–24.

33. Intzedy L, Teoh SC, Hogan A, et al. Cytopathological analysis of vitreous in intraocular lymphoma. Eye 2008;22(2):289–93.
34. Stacchini A, Demurtas A, Godio L, et al. Flow cytometry in the bone marrow staging of mature B-cell neoplasms. Cytometry B Clin Cytom 2003;54:10–8.
35. Chan CC, Whitcup SM, Solomon D, et al. Interleukin-10 in the vitreous of patients with primary intraocular lymphoma. Am J Ophthalmol 1995;120(5):671–3.
36. Tritten JJ, Haefliger JM, Delouche D, et al. Interleukin 10 and chronic vitritis in a case of ocular lymphoma [in German]. Klin Monatsbl Augenheilkd 1998;212(5):416–7.
37. Akpek EK, Maca SM, Christen WG, et al. Elevated vitreous interleukin-10 level is not diagnostic of intraocular-central nervous system lymphoma. Ophthalmology 1999;106(12): 2291–5.
38. Wallace DJ, Shen D, Reed GF, et al. Detection of the bcl-2 t(14;18) translocation and proto-oncogene expression in primary intraocular lymphoma. Invest Ophthalmol Vis Sci 2006;47(7):2750–6.
39. van Dijk MC, Rombout PD, Boots-Sprenger SH, et al. Multiplex ligation-dependent probe amplification for the detection of chromosomal gains and losses in formalin-fixed tissue. Diagn Mol Pathol 2005;14(1):9–16.
40. Palexas GN, Green WR, Goldberg MF, et al. Diagnostic pars plana vitrectomy report of a 21-year retrospective study. Trans Am Ophthalmol Soc 1995;93:281–308; discussion 308–14.
41. Zhai J, Harbour JW, Smith ME, et al. Correlation study of benign cytomorphology and final clinical diagnosis. Acta Cytol 2008;52(2):196–200.
42. Scott IU, Flynn HW Jr, Dev S, et al. Endophthalmitis after 25-gauge and 20-gauge pars plana vitrectomy: incidence and outcomes. Retina 2008;28(1):138–42.