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Retinal detachment in patients with acquired immunodeficiency syndrome*

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Abstract. Cytomegalovirus retinopathy is the most frequent opportunistic infection of the eye in patients with acquired immunodeficiency syndrome (AIDS). We studied 71 patients with cytomegalovirus retinopathy ($n=69$) or acute retinal necrosis ($n=2$) with respect to the frequency and management of retinal detachment. Retinal detachment was seen in 14 patients (relative frequency, 19.7%). In 2 patients, the retinal detachment was bilateral. In 5 patients, pars plana vitrectomy and silicone-oil tamponade was performed, and in 1 of these patients scleral buckling was applied before vitrectomy. In 3 other patients scleral buckling was performed, and 1 of these individuals had sulfur-hexafluoride injection. In 8 eyes (6 patients), retinal detachment occurred in eyes with completely burned-out retinopathy without relevant function, and no surgical treatment was performed. Long-term retinal reattachment was seen in all 5 patients undergoing pars plana vitrectomy with silicone-oil tamponade. Visual acuity was preserved until the last follow-up in 4 of these 5 patients. In the patients undergoing a buckling procedure alone, no anatomic or functional success was observed. During vitrectomy, reduced retinal vascular perfusion and blood-flow sludging was observed in 2 patients. As the duration of survival of patients with AIDS and cytomegalovirus retinopathy or acute retinal necrosis is increasing, more cases of retinal detachment will be observed. Overall, 5% of patients with AIDS are expected to develop retinal detachment. In conclusion, treatment of cytomegalovirus-associated retinal detachment by pars plana vitrectomy with silicone-oil tamponade seems to be successful and safe and may maintain the patient's quality of life.

Key words: Retinal detachment – AIDS – Pars plana vitrectomy – Cytomegalovirus retinopathy – Acute retinal necrosis – Microcirculation

Zusammenfassung. Die Zytomegalievirusretinopathie (ZMVR) ist die häufigste opportunistische Infektion am Auge bei AIDS-Patienten. Wir untersuchten 71 Patienten mit ZMVR ($n=69$) oder einem akuten Retinaneekrosesyndrom ($n=2$) bezüglich der Häufigkeit und der Therapie einer Ablatio retinae. Eine Ablatio retinae war bei 14 Patienten festzustellen (relative Häufigkeit 19,7%). Bei 2 Patienten war die Ablatio bilateral. Bei 5 Patienten wurde eine Pars-plana-Vitrektomie mit Silikonöltamponade durchgeführt, und bei einem dieser Patienten wurde zuvor eine eindellende Operation durchgeführt, die bei einem Patienten mit einer SF₆-Eingabe kombiniert wurde. Bei 8 Augen (6 Patienten) trat eine Ablatio retinae in einem Auge mit vollständig ausgebrannter Retinopathie auf. In diesen Fällen wurde keine chirurgische Intervention gewählt. Bei den 5 Patienten mit einer Pars-plana-Vitrektomie und Silikonöltamponade war ein anatomischer Langzeiterfolg nachzuweisen. Die Funktion des Auges konnte bei 4 der 5 Patienten erhalten werden. Bei den 3 Patienten mit einer alleinigen eindellenden Operation war weder ein anatomischer noch ein funktioneller Erfolg nachzuweisen. Während der Durchführung der Vitrektomie konnte bei 2 Patienten ein reduzierter retinaler Perfusionsdruck nachgewiesen werden. Da die Überlebenszeit bei Patienten mit AIDS und ZMVR oder akutem Retinaneekrosesyndrom aufgrund verbesserter therapeutischer Möglichkeiten ansteigt, ist eine Zunahme der Zahl von AIDS-Patienten mit Ablatio retinae zu erwarten. Insgesamt dürfte die zu erwartende Häufigkeit bei 5% liegen. Eine Pars-plana-Vitrektomie mit Silikonöltamponade scheint eine sichere Methode zu sein, stellt bei gegebener Indikation die Therapie der Wahl dar und kann die Lebensqualität des Patienten erhalten.

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Schlüsselwörter: Ablatio retinae – AIDS – Pars-plana-Vitrektomie – Zytomegalievirusretinopathie – akutes Retinaneekrosesyndrom – Mikrozirkulation

Introduction

Cytomegalovirus retinopathy is the most common opportunistic infection of the eye in patients with acquired immunodeficiency syndrome (AIDS). This retinopathy occurs in 20%–35% of patients with AIDS, usually at the more advanced stages of the disease, when the absolute CD4⁺ helper-cell count drops below 75 cells/ μ l [27, 29, 31, 41]. Other retinal diseases in patients with AIDS include choroidoretinal toxoplasmosis, choroidoretinal mycobacteriosis, choroidoretinal *Pneumocystis carinii* infection, frosted branch angiitis, a presumed AIDS-specific zoster-associated retinopathy, and acute retinal necrosis [8, 20, 35]. Of these diseases, cytomegalovirus retinopathy and acute retinal necrosis are often associated with retinal detachment [10, 31].

Treatment with intravenously injected ganciclovir or foscarnet controls cytomegalovirus retinopathy successfully in most cases, and appears to prolong the median duration of survival from approximately 1 to 2.5 months in untreated patients up to 8–12 months in treated patients [4, 19, 24, 28, 29, 46, 47]. As the duration of survival of patients with AIDS and cytomegalovirus retinopathy or other retinal diseases increases, complications such as retinal detachment become more frequent. The purpose of this study was to estimate the frequency of retinal detachment in these patients and to evaluate the different forms of surgical repair.

Patients and methods

A total of 71 patients suffering from AIDS and viral retinopathy were studied. The diagnosis of cytomegalovirus retinopathy or acute retinal necrosis was made by indirect ophthalmoscopy. Patients were diagnosed as having AIDS according to the Centers for Disease Control definition, and all patients were positive for human immunodeficiency virus type 1 (HIV) antibodies as confirmed by Western-blot immunoelectrophoresis. In all, 68 of 70 men reported a homosexual or bisexual orientation, and 2 were i.v. drug addicts. The woman was an i.v. drug addict. According to our routine protocol, patients who had retinopathy with no sign of activity were examined monthly, and patients with signs of active retinopathy were examined every 2 weeks or every week depending on the disease activity. The mean age was 39.3 years (SD, 10.9 years). The mean absolute CD4⁺ lymphocyte count at the diagnosis of retinopathy was 25.4 cells/ μ l (SD, 13.8).

In all 14 patients with retinal detachment, prospective data were collected at the time of retinal surgery and at each subsequent ophthalmic examination. In 8 of these patients, the visual acuity before the occurrence of retinal detachment was 0.2 or better and the Karnofsky score was better than or equal to 40 [34]. Therefore, an operative approach was expected to be of benefit for these 8 patients, and a scleral buckling procedure or pars plana vitrectomy with silicone-oil tamponade was performed. The type of the procedure was determined by the surgeon.

Four eyes underwent scleral buckling procedures. In one case, additional insufflation of the long-acting inert gas sulfur hexafluoride was performed. The four rectus muscles were isolated after a limbal peritomy. An encircling number 240 (2.5-mm) band was used in three patients together with a number 279 buckle. In one patient only a number 279 buckle was used. In this patient a rebuckling operation was performed after redetachment. In one patient, pars plana vitrectomy with silicone-oil tamponade was performed after redetachment.

Vitrectomy was performed in four patients under local anesthesia and in one patient under general anesthesia using a standard bimanual, three-port technique with 20-gauge vitrectomy surgical instruments. Removal of the posterior hyaloid from all areas of visible retina was attempted. In three cases, argon-laser endophotocoagulation was used in a triple-row fashion; 5000-centistoke oil was used as an internal tamponade and direct fluid-oil exchange was performed. Lensectomy was not needed in any case.

All patients undergoing vitrectomy had internal drainage for their subretinal fluid. Undiluted vitreous, subretinal fluid, and retina was obtained intraoperatively in three patients, and culture for HIV-1 was attempted as described earlier [17]. In two patients undergoing vitrectomy we looked for retinal vascular abnormalities, and a crude estimation of the retinal vascular perfusion pressure was obtained by varying the height of the intraocular infusion bottle.

For statistical analysis, data were entered into a data base using a data-management program on a personal computer. No test for statistical significance was computed because of the small sample size. Survival duration and the time between points of interest were calculated by the Kaplan-Meier method [33] using the SPSS/PC + 5.0 package (SPSS Inc., Chicago). The relative frequency of retinal detachment was calculated by dividing the number of patients with retinal detachment (only the first affected eye and no redetachment was considered) by the number of patients of interest.

Results

In all, 14 of 71 patients with AIDS and retinopathy developed retinal detachment. This accounts for a frequency of 19.7%. In 12 patients the retinal detachment occurred after cytomegalovirus retinopathy, and in 2 patients it developed after acute retinal necrosis. In patients with cytomegalovirus retinopathy the relative frequency of retinal detachment was 17.4%. Bilateral retinal detachment was seen in 2 patients with bilateral cytomegalovirus retinopathy.

Complete long-term retinal reattachment was seen in all 5 patients undergoing pars plana vitrectomy with silicone-oil tamponade (Table 1). In 1 of these 5 patients an unsuccessful buckling operation was performed prior to vitrectomy with silicone-oil tamponade. The visual acuity (with best correction) measured at 1 month after surgery was improved in all 5 patients undergoing pars plana vitrectomy with silicone-oil tamponade. At the 3-month follow-up, the visual acuity had remained stable in 4 patients and had worsened from 0.4 to 0.2 in 1 patient. This patient had the shortest survival duration of our patients undergoing vitrectomy with silicone-oil tamponade. Nevertheless, the visual acuity was equal to or better than 0.2 in all 5 patients during the observation period. After the surgery, 1 patient used contact lenses and 2 patients wore glasses to correct the hyperopic shift. Mild subcapsular cataract formation was observed in 2 cases.

In 4 patients a buckling operation was performed; in all cases, redetachment occurred within 3 weeks. In 1 of these patients a second buckling operation was performed and redetachment was seen again within 3 weeks. In another of these patients, pars plana vitrectomy was performed in the next step, resulting in a stable reattachment with silicone-oil tamponade.

The overall success rate (long-term stabilization or improvement of visual acuity) was 4 of 5 patients treated with pars plana vitrectomy. No patient undergoing a

Table 1. Summary of cases and functional and surgical results in patients with AIDS and retinal detachment

| Case | Eye | Retinopathy | Treatment | Initial VA | Intervention | VA at last follow-up | Anatomic success |
|------|-----|-------------|-----------|------------|-------------------|-----------------------|------------------|
| 1 | OD | CMV | G | 0.4 | Buckle, ppV & Oil | 0.3 | Attached |
| 2 | OS | CMV | G/F | 0.6 | ppV & Oil | 0.8 | Attached |
| 3 | OS | CMV | G | 0.2 | ppV & Oil | 0.2 | Attached |
| 4 | OD | CMV | F, I | 0.6 | ppV & Oil | 0.8 | Attached |
| 5 | OD | CMV | G | 0.2 | ppV & Oil | 0.3 | Attached |
| | OS | CMV | | Nulla lux | – | Nulla lux | – |
| 6 | OD | CMV | G, I | 0.2 | Buckle, SF6 | HM | Detached |
| 7 | OD | CMV | G | 1.0 | Buckle (2 times) | 1.0 ^a /0.1 | Detached |
| 8 | OD | CMV | G/F | 0.3 | Buckle | 0.05 | Detached |
| 9 | OS | CMV | G | 0.2 | – | 0.2 | – |
| 10 | OD | CMV | G | 0.3 | – | 0.2 | – |
| | OS | CMV | | Nulla lux | – | Nulla lux | – |
| 11 | OD | CMV | G | HM | – | HM | – |
| 12 | OS | CMV | G | HM | – | HM | – |
| 13 | OD | ARN | A | HM | – | HM | – |
| 14 | OS | ARN | A | HM | – | HM | – |

OD, Right eye; OS, left eye; VA, visual acuity; HM, hand motions; ppV, pars plana vitrectomy; SF6, sulfur hexafluoride; CMV, cytomegalovirus retinopathy; ARN, acute retinal necrosis; G, ganciclovir; F, foscarnet; A, acyclovir; I, additional anti-CMV hyperimmunoglobulins; /, sequential therapy

^a Attached for 12 days

buckling operation had a visual acuity of 0.2 or better at 3 months after surgery.

The median duration of survival after the development of retinopathy according to a Kaplan-Meier analysis was 8.9 months ($n=71$). The median time between the occurrence of retinopathy and the development of retinal detachment was 6.2 months. The median survival duration after the occurrence of retinal detachment was 3.8 months in all patients and 6.5 months (range 1–12 months) in patients undergoing surgical treatment. The median survival after the diagnosis of cytomegalovirus retinopathy was 12.8 months in patients undergoing surgical treatment. In patients undergoing vitrectomy with silicone-oil tamponade the median survival duration after retinal detachment was 7 months (range 4–12 months).

In all, 4 patients undergoing surgery received antiviral treatment with intravenous ganciclovir (maintenance dose, 5–7.5 mg/kg daily), 1 patient received intravenous foscarnet (maintenance dose, 80–90 mg/kg daily), and 2 patients received a sequential combination of ganciclovir and foscarnet.

In 2 patients ocular perfusion was observed. Abnormal blood flow and retinal hypoperfusion was obvious as demonstrated by 2 findings:

1. A high granularity in the blood column of the major retinal vessels was present similar to the blood-flow sludging observed in conjunctival vessels in patients with AIDS. This abnormal granularity in the blood column was seen using the operation microscope and an operative contact lens before and during the surgical procedure.

2. The infusion bottle had to be located 15 inches above the body of the patient to avoid intraoperative vascular collapse, and elevation of the infusion bottle above 25 inches caused vascular collapse. The granularity in the

blood column did not change during variation of the intraocular pressure until vascular collapse occurred.

Discussion

Retinal detachment due to viral retinopathy represents a major problem in the treatment of patients with AIDS. Cytomegalovirus (CMV) retinopathy can be successfully treated in most cases with intravenously administered ganciclovir or foscarnet. However, retinal detachment may be the cause of poor visual outcome in patients with CMV retinopathy or acute retinal necrosis [6, 11, 12, 32, 39, 43, 45]. Therefore, data concerning the frequency of retinal detachment and the choice of the appropriate surgical approach are important.

In our series, five surgical procedures performed with silicone-oil tamponade were anatomically successful. On the other hand, all three surgical procedures done without silicone oil failed. This result is in accordance with the findings of Jabs et al. [32], who obtained an anatomic and functional success rate of 0% in patients undergoing a buckling procedure. The same authors report a 70% anatomic success rate in eyes undergoing pars plana vitrectomy with silicone-oil tamponade. However, functional success was observed in only 10% of their patients. The discrepancy between these findings and our results, suggesting an anatomic success rate of 100% and a functional success rate of 80%, is interesting. This difference in anatomic and functional success is probably not explainable by our small number of cases alone, because a more recent study by Regillo et al. [43] has resulted in an anatomic success rate of 100% and a functional success rate of 75%, similar to our findings.

Reports on surgical repair with silicone oil in patients with AIDS and retinal detachment due to necrotizing

retinitis other than that caused by CMV show anatomic success [10], but are less encouraging with respect to functional success [45]. Our two patients with acute retinal necrosis had a Karnofsky score of 20. Therefore, no surgical repair was attempted in these patients.

Silicone oil may cause postoperative complications such as subcapsular cataract formation, glaucoma, or keratopathy [9]. The hyperopic shift was well tolerated by all patients. One patient used contact lenses, two used glasses, and two patients accepted the change in binocularity and refractive status without correction. The only adverse effect was a mild subcapsular cataract in two cases. This finding is comparable with the results obtained by Regillo et al. [43], who reported 2 cases of cataract formation among 16 cases, and Sidikaro et al. [45], who reported similar findings. In contrast, Freeman et al. [12] reported no cataract formation and Jabs et al. [31] described only one case of cataract formation, but these observations might have been related to the relatively short follow-up periods involved.

In two patients undergoing vitrectomy we looked for retinal perfusion abnormalities. The observed high granularity in the blood column shows that blood-flow sludging in patients with HIV disease is not limited to conjunctival vessels [7, 48]. Additionally, retinal perfusion pressure was obviously reduced in both patients as measured by the hydrostatic change of the infusion bottle during vitrectomy. Recently, Dugel et al. [6] reported similar changes in retinal perfusion pressure. However, they did not report granular blood flow in retinal vessels that was similar to conjunctival sludge. Retinal microvascular changes occur frequently in patients with HIV disease, and cotton-wool spots are the most frequent manifestation of HIV-related retinal microangiopathic syndrome [13, 27]. Recently, we demonstrated a close association between the number of cotton-wool spots and reduced cerebral perfusion in patients with HIV disease [22]. Moreover, a close association between retinal microvascular abnormalities and cognitive deficits or retinal dysfunction has been described [18, 21]. Taking into account these studies, the finding of a reduced retinal perfusion pressure in patients with AIDS provides additional evidence for the hypothesis that microvascular

changes are an important factor in the pathogenesis of functional ocular and cerebral deficits in patients with HIV disease.

The results of different studies on the frequency of retinal detachment in patients with AIDS are summarized in Table 2. The frequency of retinal detachment in patients with AIDS and CMV retinopathy or necrotizing retinitis varies between 15% and 29%. This observation is in accordance with our data showing a frequency of 19.7%. Overall, given a frequency of 25% for the development of viral retinopathy in patients with AIDS [31, 40, 41] and a frequency of 20% for the development of retinal detachment, the expected frequency of retinal detachment in patients with AIDS should be 5%.

The expected frequency of retinal detachment in patients with AIDS seems to be considerably high. Therefore, the safety of surgical repair should be briefly discussed [25]. The estimated risk for infectious HIV transmission by needle puncture injuries is estimated to be 4 per 1000 [2]. HIV type 1 has been found in blood [5], different ophthalmologic tissues [16, 44], and tears by most, but not all, authors [14, 15, 17, 49]. Parenteral exposure to blood, tears, and ocular tissue might occur as well as needle puncture injuries [3, 42]. The reported rate of glove perforations in ophthalmic surgery varies between 0.3% and 15% [37, 38, 42]. These figures are lower than those reported for other surgical subspecialties [23, 30]. Wearing double gloves reduces the frequency of glove perforations in other surgical specialties, and the perforation of inner gloves is significantly lower than that of outer gloves [1, 23, 36].

Vitrectomy with silicone-oil tamponade was well tolerated by our patients, suggesting the maintenance of a good quality of life. This appears to be important, as survival should not be the only endpoint considered in patients with AIDS and should be discussed in relation to quality-of-life issues [26]. The median duration of survival of our patients with retinal detachment undergoing surgery (12.8 months) was longer as compared with that of patients without retinal detachment or as compared with that of an overall collective of patients with CMV retinopathy [18]. This discrepancy may have been due to our indications for surgery, including a Karnofsky score

Table 2. Retinal detachment in patients with AIDS: number of cases and frequency

| Authors | Year | Source | Patients with retinopathy | Patients with detachment | Frequency ^a (%) |
|----------------------|------|----------------|---------------------------|--------------------------|----------------------------|
| Freeman et al. [11] | 1987 | AJO | 17 | 5 | 29 |
| Jabs et al. [31] | 1989 | Archives Ophth | 46 | 7 | 15 |
| Gross et al. [24] | 1990 | Ophthalmol | 67 | 11 | 19 |
| Sidikaro et al. [45] | 1991 | Ophthalmol | 68 | 16 | 24 |
| Dugel et al. [6] | 1991 | AJO | NA | 19 | – |
| Jabs et al. [37] | 1991 | Archives Ophth | 145 | 38 | 26 |
| Orellana et al. [30] | 1991 | Ophthalmol | 170 | 31 | 18 |
| Regillo et al. [43] | 1992 | AJO | NA | 13 | – |
| Freeman et al. [17] | 1992 | Ophthalmol | NA | 24 | – |
| Present study | | | 71 | 14 | 20 |

NA, Not available

^a Relative frequency was calculated according to the published data if not concretely calculated by the authors themselves

of better than or equal to 40 and a reasonable functional visual acuity in the involved eye shortly before detachment. Our decision to perform vitrectomy with silicone-oil tamponade or a buckling operation was not based on these or any other criteria, but our patients were not randomized, and our sample size was small. Nevertheless, the survival after retinal detachment found in our study is comparable with that observed in previous studies reporting median survival periods of 3.1 months [39], 4.5 months [45], 9 months [32], or (mean) 8.5 months [12].

We conclude that retinal detachment should be expected in approximately 20% of patients with AIDS and CMV retinopathy. Consecutively, retinal detachment might occur in at least 5% of patients with AIDS. Pars plana vitrectomy with silicone-oil tamponade provides the best anatomic and functional success rates. Furthermore, vitrectomy with silicone-oil tamponade appears to be a safe procedure for the patient and the surgical team. Therefore, pars plana vitrectomy with silicone-oil tamponade might be the treatment of choice for patients with AIDS and retinal detachment due to viral retinopathy. Screening programs for patients with CMV retinopathy or other virus-related retinopathies in patients with HIV disease are necessary to identify patients with developing retinal detachment.

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