Original Article

Outcome of surgery in post-cytomegalovirus retinal detachment: Experience before and in the era of highly active anti-retroviral therapy in Indian eyes

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Purpose: To evaluate the outcome of surgery for cytomegalovirus associated retinal detachment (CMVRD) in human immunodeficiency virus (HIV)-infected patients in pre-highly active antiretroviral therapy (HAART) and HAART era in Indian eyes. **Materials and Methods:** Retrospective, we reviewed medical records of all consecutive HIV patients, who underwent surgical repair for CMVRD from July 1998 to June 2011. We divided patients into two groups, i.e. group 1, pre HAART era and group 2, HAART era. We compared two groups for various parameters like visual outcome, surgical success, additional procedures, follow-up, etc., **Results:** Twenty-eight eyes of 26 patients were included; 12 eyes of the 11 patients in group 1 and 16 eyes of the 15 patients in group 2. Significant visual acuity improvement was seen in both groups. Complete anatomic success was seen in 11 eyes in group 1 and 15 eyes in group 2. One additional procedure in group 1 and 29 additional procedures were done in group 2. A mean follow-up was 16 months in group 1 and 41 months in group 2. **Conclusion:** There was no difference in outcome in pre-HAART and HAART group, except for longer follow-up and additional surgical procedures in HAART group.

Key words: Cytomegalovirus retinitis, cytomegalovirus retinitis retinal detachment, cytomegalovirus, highly active antiretroviral therapy

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Cytomegalovirus (CMV) retinitis is the most frequent intraocular infection observed in HIV-infected patients. Before the introduction of highly active antiretroviral treatment (HAART), 30% of patients with HIV developed CMV retinitis during their lifetime, but with the advent of HAART, there has been a 75% reduction in the number of the new cases of CMV retinitis.[1-4] Due to decline in HIV mortality, there is increasing prevalent population of patients with CMV retinitis. CMV-associated retinal detachment (CMVRD) is one of the commonest complications following CMV retinitis. Its incidence has decreased by 60 to 77% in the western world.[5] Overall, the rate of retinal detachment (RD) in the HAART era is 0.06/person-years versus 0.33/person-years in the pre-HAART period.[6] However, in case of the patients receiving HAART with CD4 count < 50, this incidence of RD remains same as in the pre-HAART era (0.30/person-years).[6] With treatment, retention of ambulatory vision was documented even in pre-HAART era, when patients were manifestly dying of HIV.[7] In the HAART era too, result of surgery is satisfactory, although the achievement of successful visual outcome is limited.[8]

Studies from India showed that incidence of the CMV retinitis have not decreased following HAART.[9] Banker *et al*., reported that incidence of the CMVRD has further increased in their study.[9] In a prospective study done in India by Gharai *et al*., RD was seen in 70% of CMV retinitis cases in the era of HAART.[10] There is a lacuna in available literature from this part of the world, i.e. India regarding the results of reattachment surgery.

In the current study, we evaluated the results of surgery for CMVRD in HIV patients and further evaluated for any change in outcome in pre-HAART and HAART era in north India.

Materials and Methods

We conducted a retrospective analysis of medical records of all consecutive HIV-positive patients, who underwent surgery for CMVRD from July 1998 to June 2011 at our tertiary care hospital in north India. Ethics committee clearance was obtained.

The medical records of all patients were reviewed and the following data was recorded: Age and gender, characteristics of RD and CMV lesion, treatment modalities, CD4-positive T-cell count, preoperative and postoperative visual acuity (VA), proliferative vitreoretinopathy (PVR), type of tamponade (silicon oil or C3F8 gas), intraoperative and postoperative complications, status of retina (at last follow-up), and duration of follow-up. In the postoperative period, details of all additional procedures that patient underwent for visual rehabilitation were recorded. The 1991 updated classification of RD with PVR was used for the classification of PVR.[11]

We divided these patients into two groups, i.e. group 1 included pre-HAART eyes (till Dec 2004) and group 2 included eyes in HAART era (Jan 2005 onwards). We compared the two groups for visual outcome, surgical success, additional procedures, and duration of postoperative follow-up.

All the surgeries were done by two surgeons (AG and RS). All patients underwent a standard 3-port 20-gauge pars plana vitrectomy (PPV) under local anesthesia. Surgical steps included removal of the posterior hyaloid membrane with release of all retinal traction, drainage of sub retinal fluid, fluid-air exchange, endolaser photocoagulation, or

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cryoretinopexy around the retinal breaks followed by C3F8 gas or silicon oil tamponade (SOT). Also, 360° endolaser was done at the atrophic edge and normal retina. Scleral buckle (SB) was not applied in any of the cases. Lensectomy or cataract extraction was done, wherever required as a concomitant procedure.

Complete anatomic success was considered if the whole retina reattached after the surgery, and the term "partial success" was used if the macular area attached but the peripheral inferior retina remained detached.

Statistical analysis

Independent sample Student tests were used to compare group differences for continuous variables.

Results

A total of 28 eyes of 26 patients were included in study. The male to female ratio was 21:5 and the mean average age at time of diagnosis of RD was 32 years (31 years males, 34 years females). Out of 28 eyes, 22 had RD at presentation. In rest of the 6 eyes, 4 had zone 1 disease and 2 had zone 3 disease before the development of RD. Total RD was seen in 23 eyes, while 5 eyes had partial RD. Macula was attached in two eyes. Median CD4 counts were 38 cells/μL (mean 30 cells/μL, range 23-98). Associated PVR was observed in 2 eyes in HAART era [Table 1].

Twelve of the 11 patients were operated in group 1. The male: female ratio was 9:2 and the mean average age at the time of diagnosis of RD was 31 years (29 years males, 32 years females). Out of 12 eyes in group 1, all had RD at presentation, with total RD in 9 and partial RD in 3 eyes. Macula 'ON' RD was seen in one eye. Median CD4 counts were 42 cells/μL (mean 36 cells/μL, range 23-98) [Table 1]. PVR was not associated with RD in any eye in group 1. PPV with SOT was done in all eyes, except one that underwent PPV and C3F8 tamponade for superior macula 'on' RD. None of the eyes was subjected to intraoperatively lensectomy or cataract extraction.

Pre-operative VA ranged from hand motions close to face (HMCF) to 20/800 in group 1. All eyes had inactive CMV retinitis scars with RD. Follow-up in this group ranged from 3 to 96 months. Median CD4 counts were 56 cells/μL (mean 76 cells/μL, range 42-412) at the last follow-up visit [Table 2]. All except one patient lost to follow-up (9 deaths, 2 unknown). One patient who underwent PPV with gas tamponade and cataract surgery later is still under follow-up. Her CD4 counts were 412 cells/μL at the time of last follow-up. Complete anatomic success was seen in 11 eyes and partial success was seen in 1 eye. None of the eyes had recurrence of RD or required further surgery. One eye underwent cataract surgery for visual rehabilitation. Postoperative VA at the last follow-up showed significant improvement from pre-operative VA. It ranged from counting fingers at one feet to 20/160 [Table 3].

In group 2, 16 of 15 patients were operated in group 2. The male to female ratio was 12:3 and the mean average age at the time of diagnosis of RD was 30 years (29 years males, 32 years females). Ten eyes of 9 patients had RD at presentation, with one patient having bilateral RD. Out of these patients presenting with RD, 3 were put on HAART after the diagnosis of CMVRD and six were already on HAART. Rest of the 6 patients developed unilateral RD during course of treatment. These patients were already on HAART and anti-CMV therapy (systemic and maintenance intravitreal ganciclovir treatment), when they developed RD. Rest 10 eyes presented with RD, following CMV retinitis.

Table 1: General characteristics of cytomegalovirus-associated rhegmatogenous retinal detachment in HIV-positive patients at the time of surgery

Characteristic	Pre HAART (*n*=12)	HAART (*n*=16)
Median age (years)	32	29
Male/female	9/2	12/3
Unilateral/Bilateral	10/1	14/1
Median interval between RRD and surgery (days)	30	28
Mean CD4 counts at the time of RD cells/μL (range)	42 (23-98)	38 (29-84)
Preoperative LogMAR visual acuity (mean±SD)	2.55±0.57	2.11±0.58
Associated PVR (eyes)	Nil	2

CFCF: Counting fingers close to face, HMCF: Hand motions close to face, PVR: Proliferative vitreoretinopathy, SD: Standard deviation, HAART: Highly active antiretroviral therapy, RRD: Rhegmatogenous retinal detachment

Table 2: Postoperative characteristics of cytomegalovirus associated rhegmatogenous retinal detachment in HIV-positive patients

Characteristic	Pre HAART (*n*=12)	HAART (*n*=16)
Mean follow up (months±SD)	16.09±26.33	41±25.93
Postoperative LogMAR visual acuity (mean±SD)	1.56±0.48	1.29±0.70
Anatomical success (complete/partial)	11/1	15/1
Lost to follow-up (patients)	11	3
Additional procedures	1	29
Cataract surgery (eyes)	1	13
BSK removal (eyes)	Nil	3
Silicone oil removal (eyes)	Nil	2
Yag capsulotomy (eyes)	Nil	11
Mean CD4 counts at last follow-up cells/μL (range)	76 (42-412)	170 (115-350)

BSK: Band shaped keratopathy, SD: Standard deviation

Table 3: Postoperative visual acuity of cytomegalovirus-associated rhegmatogenous retinal detachment in HIV-positive patients

Visual acuity	Pre HAART (*n*=12) (%)	HAART (*n*=16) (%)
<20/400	6 (50)	2 (12.5)
≥20/400 to <20/200	4 (33.3)	10 (62.5)
≥20/200	2 (16.66)	4 (25)

Total RD was seen in 14 eyes and partial RD was seen in 2 eyes in group 2. Macula was detached in all but one eye. Median CD4 counts were 38 cells/μL (mean 32 cells/μL, range 29-84) [Table 1]. Two eyes with RD had associated PVR. All eyes underwent PPV with SOT. Two eyes underwent lensectomy intraoperatively. Preoperative VA ranged from HMCF to 20/400. Follow-up ranged from 6 to 78 months [Table 2]. Complete anatomic success was seen in 15 eyes and partial success was seen on 1 eye. There was no recurrence of RD or need for further surgery. Twenty-nine additional procedures were done for visual rehabilitation in follow-up period. Thirteen eyes underwent cataract surgery with IOL implantation. Eleven of these underwent YAG capsulotomy also. Three eyes had band shaped keratopathy (BSK) removal. Silicone oil removal (SOR) was done in 2 eyes with successful outcome [Table 2]. Postoperative VA at the last follow-up showed significant improvement from pre-operative VA. Postoperative VA at last follow-up ranged from HMCF to 20/80 [Table 3]. All except 5 patients are under regular follow-up (5 patients expired). Median CD4 counts were 156 cells/μL (mean 170 cells/μL, range 115-350) at the last follow-up visit [Table 2].

Discussion

Our study showed that the visual prognosis of CMVRD has not changed in the HAART era. Once RD occurs in these eyes, prognosis is same in both eras after treatment. In HAART era, increased survival of patients has lead to increased number of additional procedures performed on patients. In our series in HAART era, 12 (80%) out of 15 patients were on HAART when they developed RD, representing the true picture in HAART era.

Severe visual loss (defined as a loss of more than 6 lines of the ETDRS chart) was significantly associated with the occurrence of RD (69% of the eyes with RD vs. 8% of the eyes without RD) in CMV retinitis eyes.[12] Once RD occurs, surgical management of RD is required to prevent further visual loss. The surgical options used for CMVRD include PPV with SOT or gas tamponade, laser photocoagulation, pneumatic retinopexy, and SB or combination of these. However, given the unique nature of these RD's and known efficacy of PPV and SOT, it is preferred method of repair of CMV-associated RD.[13,14] In this series, PPV with gas tamponade was done in one eye with superior RD with large posterior break in group 1. PPV with SOT was done in rest of the eyes.

Various reports on surgical treatment showed a high degree of variability in visual outcome, even in eyes with successful anatomic attachments.[7,13-18] Our results exhibited similar anatomic success in both groups. Complete anatomic reattachment was seen in 92.31% in total eyes (91.66 in pre HAART and 93.33 in HAART era). However, macular attachment could be achieved in all eyes in both groups with SOT. Davis and associates showed anatomical reattachment rate of 73% completely attached and macula attached in 94% at the final follow-up in HIV patients with RD secondary to necrotizing retinitis.[7]

In our series, VA of ≥ 20/400 was achieved in 71.42% of total eyes (50% in pre HAART and 87.5% in HAART era). We observed better visual outcome in HAART era. We believe that this has nothing to do with the HAART. It was strongly related to preoperative VA as this phenomenon was also noticed by others.[13,15,18] Pre-HAART group had postoperative VA < 20/400 in 50% of the eyes, preoperatively 66.65% of eyes in this group had HMCF vision. HAART group had postoperative VA < 20/400 in 12.5% of the eyes, preoperatively, 25% of eyes in this group had HMCF vision.

Recently, PVR has also been added to this list for poor visual prognosticators in HAART era. Kunavisarut *et al*., reported 29% PVR at the time of first surgery and associated it with higher CD4 counts and longer interval between diagnosis of RD and surgery.[18] In our series, we reported PVR in 2 (7.14%) eyes of 2 patients already on HAART. Their respective CD4 counts were 72 and 84 cells/μL. The cause of low incidence of PVR in this series can be attributed to low CD4 counts and low interval between diagnosis and surgical treatment. We did see immune recovery uveitis (IRU) in one of these eyes after surgery when CD4 improved during follow-up. Our anatomic success was also better in view of low rate of PVR. Kunavisarut *et al*., reported 40% redetachment in eyes with PVR as compared to 0% in no PVR group.[18]

The introduction of HAART has significantly increased the survival of patients with the CMV and HIV.[19] Before its widespread use, the median survival time after PPV and SOT was 4 months.[20] In our series, all except one pre-HAART era patients lost to follow-up due to high mortality in pre HAART era. However, median survival rate was 12 months and 66.6% patients of the HAART era patients in this series are still under follow-up.

With increased longevity of these patients, these eyes require additional procedures for optimal visual rehabilitation such as cataract surgery, YAG capsulotomy, and silicon oil removal. Tanna *et al*., reported high incidence of cataract after surgery with SOT for CMVRD and posterior capsular opacification (PCO) occurred rapidly in these eyes.[21] In our series in HAART era, all 13 eyes underwent cataract surgery with IOL implantation within 1 year of undergoing PPV. Out of these 13 eyes, 11 had undergone YAG capsulotomy for PCO. One patient from pre-HAART also underwent cataract surgery 5 years after PPV.

In these SOT eyes, for optimizing vision and to prevent other complications due to silicon oil, SOR is required eventually.[22] Morrison *et al*., reported 50% redetachment rate in post SOR eyes. In our series, till now, we have done 2 SOR without any re-RD.[23] Recently, Dave *et al*., from India reported results of SOR in CMVRD.[24] They showed success rate of 81.82% out of the 11 eyes who underwent SOR. None of our cases underwent simultaneous cataract extraction. We did simultaneous BSK removal with EDTA in these two eyes. The third eye, where we did BSK removal, was that of a one-eyed young man with 20/400 useful vision. We encountered less SOR-related complications in this series. We routinely use high viscosity silicon oil (5000 centistoke) in all cases in HAART era.

Apart from being a retrospective study, our study has many limitations. All these above issues in pre- and HAART era are well studied and published from the industrialized world. Major HIV population lives in Asia and Africa. There are only few studies from the East Asian countries addressing these issues. There is lack of literature on these issues from this part of the world. Recently, Dave *et al*., in their series from South India, showed results of SOR in CMVRD.[24] In their

series, they showed that 61.66% of the patients did not come for follow-up and recurrent detachment in 12 eyes. Banker *et al*., and Gharai *et al*., reported high incidence of CMVRD in our population.[9,10] This can be attributed to unavailability of HAART, inadequacy of HAART, and resistant or intolerance of HAART. One of the primary factors in our population is poverty, illiteracy, and lack of knowledge about the disease leading to lots of missed follow-ups and non-compliance to treatment. All these factors lead to inadequate treatment of HIV and its associated infections. Gharai *et al*., has shown that incidence of CMV retinitis has not decreased in HAART era in India in the absence of affordable anti-CMV therapy.[10] As CMV retinitis and its complications remain to be a health issue in our country, it is relevant to know the results of its management in our own population.

Our study shows that there was no difference in the outcome of the re-attachment surgery in pre- and HAART era group, except for additional surgical procedures in the HAART group. Once the RD develops, the prognosis is the same in HAART eyes. Furthermore, in the HAART era, because of longevity of AIDS patients, more patients require interventions other than RD surgery alone.

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