Shrestha and Manandhar
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Original Article

Clinical Profile and Treatment Outcomes of Acute Retinal Necrosis in a Tertiary Eye Care Centre in Nepal

Priyanka Shrestha[1], Anu Manandhar[2]

[1]Department of Ophthalmology, Kathmandu Medical College Teaching Hospital, Kathmandu, Nepal
[2]Tilganga Institute of Ophthalmology, Kathmandu, Nepal

ABSTRACT

Introduction: Acute retinal necrosis (ARN) is a rapidly progressive, necrotizing herpetic infection, commonly leading to retinal detachment with significant visual morbidity. Most common causative agent belong to the herpesvirus family. It commonly occurs in healthy immunocompetent individuals. Early diagnosis of disease is important in order to start the treatment timely. Systemic antivirals and intravitreal antiviral therapy along with steroids are the main stay of treatment. Our study is a retrospective study of 5 years. We studied the patient demographics, presenting features, treatment outcome and complications of acute retinal necrosis in a tertiary care center in Nepal.

Objective: Methodology: A total of 14 eyes of 13 patients were included in the study. This study is a hospital based retrospective study done in the Uveitis and Vitreoretinal department of a tertiary eye care center. Records of all patients diagnosed with Acute Retinal Necrosis between May 2013 to May 2018 were included in this study. Hospital data of these subjects including patient demographics, presenting symptoms, clinical signs, treatment received and treatment outcome were noted and analysed.

Result: The mean age of the patients was 45.1 years ± 14.9 years. Sixty-nine were males and 92.3% had bilateral involvement. The mean duration of onset of symptoms was 22.4 days ± 19.5. The most common presenting symptom was decreased vision (78.6%). Among the 13 patients 10 received intravenous acyclovir, 1 received intravenous ganciclovir and 2 patients received oral acyclovir for initial systemic therapy.

Conclusion: The most common complication was cataract followed by retinal detachment.

Key words: Acute retinal necrosis; acyclovir; herpes.

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Corresponding Author
Dr. Priyanka Shrestha
Department of Ophthalmology,
Kathmandu Medical College Teaching Hospital,
Email: priyankashresthapradhan@gmail.com

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INTRODUCTION

Acute retinal necrosis (ARN) was first described in 1971 characterised by rapidly progressive, necrotizing herpetic infection, commonly leading to retinal detachment with significant visual morbidity. (A. Urayama, N. Yamada, T. Sasaki, 1971) Mostly it is unilateral and in some cases becomes bilateral. (Dorman and Donaldson, 2018) Causative agents of acute retinal necrosis belong to the herpesvirus family , the most common being Varicella Zoster virus followed by the Herpes Simplex virus 1 and 2, Cytomegalovirus and Epstein-Barr virus. (Anthony, Bavinger and Yeh, 2020) ARN comprises of acute confluent peripheral necrotizing retinitis, vitritis and retinal arteritis. It commonly occurs in healthy immunocompetent adults. It may be associated with granulomatous anterior uveitis, episcleritis, disc edema , ocular pain and variable degree of visual loss. (Blumenkranz *et al.*, 1986) There is no gender or age predilection (Mayer *et al.*, 2022) however a genetic association in Caucasian patients with HLA -Dw7 antigen and HLA-Bw62 phenotype has been found. (Anthony, Bavinger and Yeh, 2020) Early diagnosis of the disease is important in order to start the treatment timely. Newer oral antivirals have greater bioavailability and can be used as first line oral therapy. Intravenous antivirals are also being used. Intravitreal antiviral therapy helps in providing immediate intravitreal drug levels as compared to systemic therapy. (Schoenberger *et al.*, 2017) The use of systemic antiviral acyclovir has found to decrease the involvement of fellow eye. (Tibbetts *et al.*, 2010) Our study is a retrospective study of 5 years where we studied the patient demographics, presenting features, treatment outcome and complications of acute retinal necrosis in a tertiary care center in Nepal.

METHODOLOGY

This study is a hospital based retrospective study done in the Uveitis and Vitreoretinal department of Tilganga Institute of Ophthalmology. Records of all patients diagnosed between May 2013 to May 2018 were included in this study. Ethical clearance from Institutional Review Committee of Tilganga Institute of Ophthalmology was taken (Ref: 06/2018).

Standard diagnostic criteria proposed by the American Uveitis Society in 1994.(Holland and Executive Committee of the American Society of Uveitis, 1994) The criteria is as follows:

1. One or more focus of retinal necrosis in peripheral retina having discrete border (primarily involving areas adjacent to or outside the major temporal vascular arcades. Macular lesions are less common but does not preclude a diagnosis of ARN if they are present along with the peripheral lesions)
2. Rapid disease progression in absence of antiviral therapy
3. Circumferential spread of disease
4. Occlusive vasculopathy with arteriolar involvement
5. Prominent inflammation in the vitreous and anterior chamber
6. Other characteristics that support but are not required for diagnosis are: optic neuropathy/ atrophy, scleritis and pain

Hospital data of all subjects diagnosed as ARN on the basis of above criteria in the

above mentioned 5 years were included in the study. The patient demographics, presenting symptoms and clinical signs were noted. Parameters like presenting BCVA and final BCVA following treatment was analysed with the help of Snellen chart. Best corrected visual acuity was used and was recorded in Snellen acuity. Snellen visual acuity was then converted to LogMAR units. Poor vision like counting fingers , hand motions, perception of light and no PL were substituted with 2.10, 2.40, 2.70 and 3.00 LogMAR respectively. (Day *et al.*, 2015; Moussa, Bassilious and Mathews, 2021)·(Cai *et al.*, 2020) Also other parameters like anterior chamber inflammation, vitreous involvement, retinal involvement, treatment done and complications were analysed as well. The data was entered in MS excel 2019 and analysis was done using SPSS software.

RESULT

A total of 14 eyes of 13 patients were diagnosed with acute retinal necrosis during the duration of 5 years. Two patients (15.3%) were diagnosed as Acute Retinal Necrosis in the year 2013 and 2017, 4 (30.7%) patients were diagnosed as acute retinal necrosis in the year 2015 and 2018 and 1(7.7%) patient was diagnosed as acute retinal necrosis in the year 2016. The mean age of the patients was 45.1 years ± 14.9 (Range 22-69 year). The distribution of patients according the age range is given in Table 1.

There were 4 females (30.7%) and 9 males (69.2%). Fourteen eyes of 13 patients were included. Among the patients 1(7.7%) had bilateral involvement and 12 (92.3%) have unilateral involvement. The patient who had bilateral involvement the gap between the involvement of two eyes was one and half months. Depending on the eye involved, 10 (71.4 %) were left eye and 4 (28.6%) were right eye. The mean duration of onset of symptoms was 22.4 days ± 19.5 (Range 4- 75 days). Distribution of the patients depending on the duration of onset of symptoms is given in Table 2.

Table 1: Distribution of the patients according the age range

Age range	Number of patients	Frequency (%)
20-30	3	23.1
31-40	2	15.4
41-50	3	23.1
51-60	2	15.4
61-70	3	23.1
Total	13	100

Table 2: Distribution of the patients depending on the duration of onset of symptoms

Duration of symptoms (in days)	Number of eyes	Frequency (%)
1-7 days	3	21.4
8-14 days	4	28.6
15-21 days	2	14.3
22-28 days	0	0
>28days	5	35.7
Total	14	100

Most of our cases presented during summer (n= 6, 46.1%) and spring season (n=4, 30.7%) followed by 2 (15.4%) cases in autumn and 1 (7.7%) cases in winter.

Distribution of symptoms among patients diagnosed with acute retinal necrosis is given in Table 3.

Distribution of presenting best corrected visual acuity in the patients is given in Table 4:

Maximum number of patients has vision less than 1/60 on presentation. Five of them had hand motions, 2 of them had counting finger close to face and 2 of them had perception of light. One of the patients has inaccurate projection of rays on presentation. The mean LogMAR visual acuity after conversion of Snellen unit to LogMAR was 1.86 ± 0.84. Four of the patients (21.4%) had decreased corneal sensation. Distribution of patients depending on anterior chamber inflammation (on the basis of SUN classification) and vitreous haze (NIH grading) is shown in table 5.

Table 3: Distribution of symptoms among diagnosed patients

Symptoms	Number	Frequency
Decreased vision	11	78.6
Photophobia	3	21.4
Redness	10	71.4
Pain	7	50

**Multiple responses*

Table 4: Distribution of presenting best corrected visual acuity

Presenting BCVA	Number of eyes	Frequency
6/6-6/18 (0-≥0.5)	2	14.3
<6/18-6/60 (<0.5- 1)	2	14.3
<6/60-3/60 (<1.0- 1.3)	0	0
<3/60-1/60 (<1.3-1.80)	1	7.14
<1/60- Perception of light (<1.8-3.0)	9	64.3
No perception of light (4.0)	0	0
Total	14	100

Table 5: Distribution of patients depending on anterior chamber inflammation (on the basis of SUN classification) and vitreous haze (NIH grading)

		Number of eyes	Frequency
Anterior chamber Inflammation	+0.5	3	21.4
	+1	6	42.9
	+2	4	28.6
	+3	1	7.1
	Total	14	100
Vitreous Haze	Grade 1	4	28.6
	Grade 2	6	42.9
	Grade 3	4	28.6
	Grade 4	0	0
	Total	14	100

The mean intraocular pressure (IOP) of the patient was 12. 4 ± 5.7 (Range 3-26 mm Hg). Maximum eyes (n=8, 57.1%) had normal IOP (11-21 mm Hg) on presentation. Five eyes (35.7%) had IOP between 1-10 mm Hg and 1(17.1%) eye had IOP greater than 21 mm Hg. Disc edema was present in only 5 (35.7%) of the eyes. Retinal involvement was classified on the basis of quadrant involvement of the retina. Five eyes (35.7 %) had 1-quadrant involvement, 2- quadrant involvement was seen in 4 eyes (28.6%), 3-quadrant involvement was seen in 1 eye (7.1%) and all 4-quadrant involvement was seen in 4 eyes (28.6%).

Intravenous Acyclovir was given to a total of 10 patients (71.4%) and 1 patient received intravenous Ganciclovir (2 doses). Two of the patients received oral acyclovir. Among the 10 patients who received intravenous Acyclovir, 4 (40%) of them received it for 5 days and remaining 60% of them received it for 3 days. Among the 14 eyes, 7(50%) of the eyes received intravitreal acyclovir. Among the 7 eyes more than half (n= 4, 57.1%) received 2 intravitreal doses, 2 (28.6%) received 1 dose and 1(14.3%) received 3 doses of intravitreal acyclovir. Six eyes (42.9%) received intravitreal Ganciclovir. Among which 2 of the eyes received intravitreal Ganciclovir after receiving intravitreal Acyclovir. Five eyes (83.3%) received 1 dose of intravitreal Ganciclovir and 1 eye (16.7%) received 2 doses of intravitreal Ganciclovir. All the patients who received intravenous acyclovir received oral acyclovir on follow up. Oral steroid was received by all patients following antiviral treatment after the patients started to show improvement of retinal lesions.

Distribution of complications in patients with Acute retinal necrosis is given in Table 6

The final visual acuity following treatment of the disease is given in Table 7

The mean final Best corrected visual acuity following treatment was 1.5 ± 0.9 LogMAR

Table 6: Distribution of complications

Complications	Number of eyes	Frequency
Cataract	10	71.4
Retinal detachment	7	50
Glaucoma	5	35.7
Retinal tear	1	7.1

**multiple responses*

Table 7: The final visual acuity following treatment of the disease

Final BCVA (LogMAR)	Number of eyes	Frequency
6/6-6/18 (0-≥0.5)	2	14.3
<6/18-6/60 (<0.5- 1)	4	28.6
<6/60-3/60 (<1.0- 1.3)	1	7.1
<3/60-1/60 (<1.3-1.80)	2	14.3
<1/60- Perception of light (<1.8-3.0)	3	21.4
No perception of light (4.0)	2	14.3
Total	14	100

DISCUSSION

Acute retinal necrosis though uncommon is a severe type of necrotizing retinitis, if not treated timely can lead to blindness. It is a viral retinitis and most commonly caused by the Varicella -Zoster virus and Herpes Simplex virus. Cytomegalovirus and Epstein Barr virus have also been found . (Ganatra *et al.*, 2000; Bonfioli and Eller, 2005) Acute retinal necrosis has an acute onset of anterior uveitis, vitreous inflammation, occlusive vasculitis, necrotizing retinitis and disc edema.(Shantha *et al.*, 2015) Racial predilection is not found in ARN.(Duker and Blumenkranz, 1991) Among the initially reported cases of ARN there was a slight male preponderance(Fisher *et al.*, 1980) which was also seen in our study where 69.2% of the patients were male. However further studies haven't shown any clear gender predilection. (Lau *et al.*, 2007; Dorman and Donaldson, 2018) Acute retinal necrosis shows a bimodal distribution in ages distribution and typically affect age group between 20 and 60 years of age.(Duker and Blumenkranz, 1991) Also, in our study the mean age of the patients was 45.1 years ± 14.9 years (range 22-69 years) which was similar to other studies done in different countries. (Lau *et al.*, 2007; Dorman and Donaldson, 2018).(Cochrane *et al.*, 2012)

Studies have shown that herpes zoster infection is seasonal with a peak in the summer (August) season(Berlinberg *et al.*, 2020) and lowest in winters.(Nozomu and Kimiyasu, 2009; Berlinberg *et al.*, 2020) A study on the seasonality of acute retinal necrosis showed higher occurrence of ARN in the winter and spring(Hedayatfar *et al.*, 2020) in contrast to our study where the occurrence was more during spring and summer . The difference could indicate the variations in seasonality of ARN in different regions however due to small sample size it cannot be generalised and requires more larger prospective studies in future.

Majority of patients in our study had unilateral involvement. Studies have shown that use of systemic acyclovir reduces the risk of fellow eye. (Palay *et al.*, 1991) Simultaneous or sequential involvement of the other eye can occur in 70% of untreated and 90% of immunocompromised patients occurring few months to years later. (Anthony, Bavinger and Yeh, 2020) All our patients had received systemic antivirals, most likely due to which none of our patients developed acute retinal necrosis in fellow eye in follow ups. The mean duration of symptoms prior to presentation was 22.4 days which was slightly higher as compared to other studies. (Dorman and Donaldson, 2018)

Acute retinal necrosis is more commonly found in patients who are immunocompetent contrasting to Progressive outer retinal necrosis which is seen in immunocompromised (Anthony, Bavinger and Yeh, 2020). However it is also seen in patients who are immunocompetent and who are under corticosteroids, immunosuppressants and chemotherapy. It has also been seen in Acquired Immune Deficiency Syndrome. (Reece and Koushik, no date) In our study none of the patients were immunocompromised.

The most common symptom among the patients diagnosed with acute retinal necrosis was diminution of vision which was present in 78.6% of the patients followed by redness (71.4%) and pain (50%). Blurring of vision is found to be the most common symptom of patients with acute

retinal necrosis in most of the studies. (Dorman and Donaldson, 2018) Patients presenting with acute retinal necrosis had very poor vision on presentation 64.2% of whom had vision less than 1/60 (log MAR 1.8) which is similar to other studies where patients with acute retinal necrosis presented with poor vision. (Mojarrad *et al.*, 2022)·(Butler *et al.*, 2017)

The mainstay of treatment for acute retinal necrosis is a combination of systemic and intravitreal therapy along with corticosteroids to control the severe inflammation seen in ARN. The most common complication of ARN is retinal detachment which can be prevented by timely barrage laser photocoagulation and pars plana vitrectomy is done to prevent retinal detachment, for obtaining a vitreous sample for diagnosis and treatment of retinal detachment. (Anthony, Bavinger and Yeh, 2020) The most commonly adopted initial treatment is intravenous acyclovir or oral valacyclovir. Other antivirals used are oral Famciclovir, Valganciclovir, Acyclovir, intravenous Foscarnet or Ganciclovir. The drug most commonly used in our setting is acyclovir due to its easy availability. (Schoenberger *et al.*, 2017) Intravitreal antivirals reduces the risk of severe vision loss and development of retinal detachment however it does not prevent the fellow eye involvement. Therefore, systemic antivirals should always be used to prevent fellow eye involvement.

Retinal detachment is a common complication of acute retinal necrosis and is one of the main causes of poor visual outcome in patients with ARN. (Hoogewoud *et al.*, 2022) Various studies have shown different rates of occurrence of retinal detachment. Rates have ranged from 25% - 70% (Shiezadeh *et al.*, 2023),(Tibbetts *et al.*, 2010) In our study the rate of occurrence of retinal detachment was 50% which was comparable to other studies. (Tibbetts *et al.*, 2010)

We have slightly deviated from the standard of care regarding intravenous acyclovir and given a shorter duration of intravenous treatment for various reasons. Intravenous Acyclovir is a costly medicine and the cost of the medicine is not covered by health insurance which restricts its use for a longer duration especially in a developing country like ours. However, we are invariably using intravitreal Acyclovir for all cases of acute retinal necrosis which increases the local drug availability and therefore helps to decrease the duration of intravenous Acyclovir. Finally, in our years of experience of treating acute retinal necrosis, the use of intravitreal acyclovir combined with shorter duration of intravenous Acyclovir, have found to be very effective in the recovery of disease. However, our small sample size and the design of the study with a lack of control group limits our ability to draw strong conclusion which are statistically significant.

CONCLUSION

Acute retinal necrosis is an uncommon viral infection without any specific racial and gender predilection. In our study 14 eyes of 13 patients were included with a mean age of 45.1 years and a male preponderance. The most common presenting symptom was decreased vision present in 78.6%. Sixty four percent of the patient presented with BCVA less than 1/60 and the final BCVA following treatment was

between 6/24 and 6/60 in maximum (42.8%) number of patients. The most common drug used for management of acute retinal necrosis in our study was acyclovir in the intravenous, intravitreal and oral form. Acyclovir has been the drug of choice for many years for the management of acute retinal necrosis. In our setting too where acyclovir is easily available and cost effective the most commonly used drug is Acyclovir. In some situations where the patient is unresponsive to acyclovir or have severe infection ganciclovir is used. Most of the patients were given 3 days of intravenous acyclovir which was found to be effective for the control of infection.

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