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Management and Outcome in Hiv Patients with Oppurtuinistic Infections

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Abstract

Background: Morbidity and mortality in HIV patients is supposed to be more due to the various opportunistic infections in them and hence management of these infections and their outcome is essential. Ocular infections may cause impairment of vision or blindness. *Aim of the Study:* To detect the outcome after management of HIV patients who presented to the department of ophthalmology with various opportunistic infections. *Materials and Methods:* A retrospective study was done on HIV patients who reported to the department of ophthalmology with various infections from June 2015 to June 2016 at Sarojini Devi Eye Hospital, Hyderabad, India. A detailed systemic and ophthalmology examination was carried out on all the patients. Demographic data, visual acuity, slit lamp examination, indirect opthalmoscopy, colour charting and CD4 count were noted from the hospital records. *Results:* We found patients with cytomegalovirus (CMV retinitis), Acute retinal necrosis (ARN), toxoplasma retino chroiditis and subretinal tuberculous abscess were usually seen in our study. Patients with good general condition responded better to our treatment. Bilaterally affected patients were more than unilateral affected ones. Elderly patients had lower CD4 count and poor general condition. *Conclusion:* There is a need for having an ophthalmologist for screening in all HARRT centres. But in circumstances where clinical findings will emulate other infections, PCR analysis can help in finding the cause.

Keywords: Acute Retinal Necrosis; CD4; Cytomegalovirus Retinitis; HIV; Gangcyclovir; PCR.

Introduction

Opportunistic infections are disease processes that affect people with weakened immune systems, otherwise do not cause any disease in a healthy host. One such condition which affects immune system is Acquired Immune Deficiency Syndrome resulting in various opportunistic infections that affect eyes, oral cavity, skin and other parts of the body causing severe morbidity and mortality due to depleted CD4 count. Common opportunistic infections seen in HIV patients are cryptococcal meningitis, toxoplasmosis, oesophageal candidiasis and ocular lesions like viral retinitis due to cytomegalovirus, herpes simples and varicella zoster [1-3].

One of the commonest cause of blindness in HIV affected individuals is CMV retinitis. It is usually seen in advanced stages of infection where CD4+ T-cell count is less than 50 cells/ml [2].

CMV retinitis caused by EDNA virus was shown to have an incidence of about 30% before 1997, but with introduction of HARRT in management of HIV patients, its incidence has been reduced. But still CMV retinitis is seen in many patients in developing countries like India. CMV can affect any system, but commonly affects gastro intestinal tract and ocular apparatus [3-5].

The patients affected show characteristic features that include vascular sheathing, haemorrhagic retinal necrosis and combined retinal detachment. The lesions are present alongside the retinal vessels giving the characteristic Pizza-Pie or Cheese-Pizza appearance with thick yellowish white infiltrates alongside the retinal vessel and retinal haemorrhages at periphery that extend in the direction of the posterior pole [2]. Clinical examination and examination of intraocular fluid by PCR are usually carried in such patients. We carried our study to detect the outcome after management of HIV patients who presented to the department of ophthalmology with various opportunistic infections [6-8].

Materials and Methods

A retrospective study was carried out on 21 HIV patients with different opportunistic infections reported to the vitreo retina department of Sarojini Devi Eye Hospital, Hyderabad, India, from June 2015 to June 2016. A detailed case history was taken and systemic examination was done for all

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the patients. After Best Corrected Visual Acuity (BCVA), a detailed ophthalmic assessment with slit lamp examination, indirect ophthalmoscopy and B Scan Ultrasonography (if media was not clear) was also done on all the subjects. Investigations including CD4 count was made in all the sample prior to treatment. Demographic data and the findings of ophthalmic examination were recorded. In all these patients fundus images were taken and intraocular fluid analysis was carried out to detect the pathogens by culture, gram stain and PCR analysis.

Patients with active retinitis in periphery and posterior pole were treated with intravitreal gangcyclovir. Injection gangcyclovir was given intra vitreally two times per week as induction therapy and weekly once as maintenance therapy till the lesion becomes dry. After the lesion becomes dry, laser was applied to the edges of lesion to prevent necrotic breaks which generally occurs at the junction of normal and atrophic healed necrotic retina. We maintained the dose based on the zone, area involved in fundus and also the severity of disease. Patient with sub retinal abscess was managed with posterior sub tenon's triamcinolone acetonide. We treated one patient who had severe, continuous retinal necrosis in both eyes, in whom anterior chamber (AC) tap showed herpes group of virus, was managed with systemic acyclovir.

Results

Our sample size was 21, among which 13 (61.9%) were females and 8 (38.0%) were males with a female to male ratio of 1.625 (Fig. 1). The age of the sample ranged between 25 to 60 years, with a mean age of 42 years. When the location or region was asked it was found that majority of them 13 (61.9%) belonged to coastal Andhra Pradesh, 6 (28.5%) from Telangana state and 2 (9.5%) from North Karnataka.

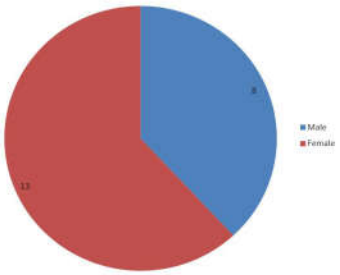

Fig. 1: Pie chart showing gender distribution.

On ophthalmic examination, the majority of the patients presented with light perception in cases of severe active retinitis and optic neuropathy. Three cases (14.2%) had no light perception in one eye owing to optic neuropathy. Two (9.5%) patients with only peripheral involvement had 6/6 vision, in three cases (14.2%) BCVA was 6/60.

Ophthalmic assessment revealed unilateral eye involvement in 6 cases (28.5%) and remaining all cases showed bilateral involvement. Two patients (9.5%) showed anterior chamber reaction with Keratic Precipitates (KPs), flare. Two (9.5%) patients had significant cataractous changes. On posterior segment examination, vitreous cells was seen in most of the patients, three patients (14.2%) showed moderate vitritis, and 5 patients (23.8%) had severe vitritis (Fig. 2).

The most common opportunistic infection in our study was CMV retinitis. It usually is categorized into four clinical types, oedematous, indolent, peri vascular and optic neuropathy, remaining clinical presentation grouped as others (Fig. 3) [7].

Five patients (23.8%) had severe active haemorrhagic retinitis and also exudative retinal detachment with massive subretinal exudation. PCR analysis done in all patients, clinically these patients fundus picture was like Progressive Outer Retinal Necrosis (PORN). Five cases (23.8%) presented with pale disc, attenuated vessels, atrophic retina in one eye and active retinitis involving the periphery and encroaching the posterior pole in the other eye (Fig. 4).

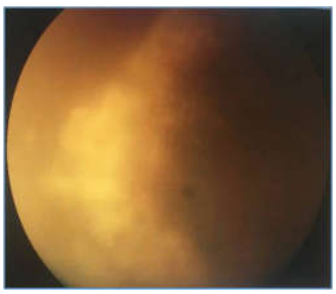

Fig. 2: Fundus details hazily seen due to severe vitritis.

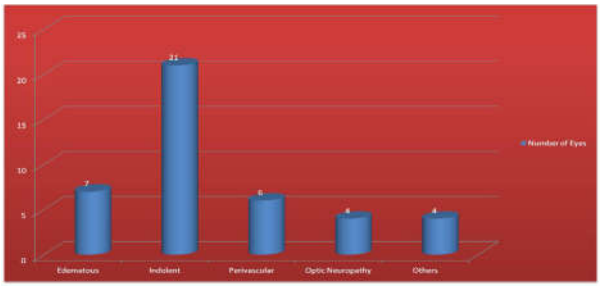

Fig. 3: Bar Graph showing number and percentage of clinical types of CMV Retinitis

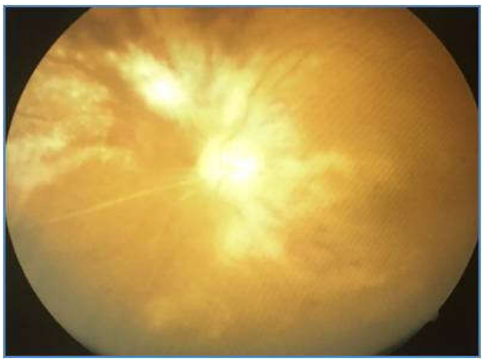

Fig. 4: Fundus image showing pale disc and confluent yellow white retina with superficial retinal haemorrhages, sclerosed vessel.

Fig. 5: Fundus image of patient showing retinitis in periphery.

Four cases (19.0%) showed typical pizza -pie appearance with frosted branch angitis in one eye and peripheral necrosed retina in one quadrant in the other eye (Fig. 5). Two patients (9.5%) had retinitis in one eye, with the other eye completely normal with 6/6 vision.

One female (4.7%) patient had combined retinal detachment in one eye and the other with healed retinitis, pigmented atrophic contiguous scars in periphery with necrotic break temporally. One female (4.7%) patient showed thinned out atrophic retina in periphery, with no vision in other eye as it was cataractous. Scan showed retinal detachment with intra retinal cystic, reminiscent of inflammatory vitreous opacities. In two patients (9.5%) there was involvement of macula in one eye and other eye was normal. In one patient (4.7%) vitritis and subretinal abscess in the inferior quadrant was seen.

Patients with localised oedematous type of CMV retinitis, after intravitreal gangcyclovir, showed good response with healing of lesion in few weeks and the visual outcome i.e. BCVA being 6/6 in them. In patients with low CD4 count with massive sub retinal exudation did not respond to the treatment, but vitritis was resolved to some extent, but the active retinitis persisted. In patients with indolent form treated with intravitreal gangcyclovir for long period showed moderate response. BCVA was CF 3mts to 6/60.

Patients who presented with pale disc, attenuated vessels were treated and explained about the prognosis. Patients with ARN due to herpes simplex were treated with acyclovir, without any response. Patients with combined exudative and rhegmotogenous retinal detachment were operated. Pars plana vitrectomy with silicone oil tamponade was carried out in them and the anatomical outcome was very bad due to exudation and thin necrotic retina. Two patients presented with rhegmatogenous retinal detachment due to small, multiple breaks in the periphery, which occurred in thin atrophic retina and were treated with pars plana vitrectomy and silicone oil tamponade. These patients anatomical was fairly good, retina attached under silicone oil, laser was done, the visual outcome was CF 2mts. BCVA was same even after removal of silicone oil.

Two patients showed macular chorio retinitis, To find out the pathogen, PCR analysis was carried out, but it did not disclose any pathogen, hence intravitreal dexamethasone and gangcyclovir were given two times per week. Towhich the response was very slow, taking about 8 weeks for resolving the lesion.

Discussion

Many opportunistic infections are seen in HIV affected individuals patients owing to the suppression of immune system. These infections are commonly seen in individuals with depleted CD4 count. Many studies have reported ocular lesions in HIV patients. We found the commonest infection as CMV retinitis which is supposed to be the most common cause of blindness in HIV patients with about 30 to 40% incidence in India [4,8-10].

We found a female preponderance, similar to the previous studies. However males showed aggressive clinical and laboratory picture of infections as well as bilateral involvement. Only one young female patient showed aggressive disease in both eyes with CD4 count 9 cells/micro litre and very poor general condition. The mode of transmission in our cases was due to sexual transmission, with the exception of one young adolescent boy who was supposed to get infected through trans placental transmission. All the opportunistic infections are thought to be due to haematogenous spread, rather than by direct entry of infective organism [11,12].

We found that majority of the sample patients reported to the department very late and end stage of the disease with almost no vision in one eye and drop in vision in the other. Some with both eyes and general condition being very bad. Hence we suggest proper counselling and awareness in HIV affected individuals regarding the likelihood of opportunistic infections and the chances of becoming blind due to ocular infections. Physicians rely on CD4 count whether to initiate HAART therapy count and literature has shown that CD4 count less than 50 cells/micro litre has higher risk of CMV retinitis. In our study many patients presented with lower CD4 counts, possibly explaining the occurrence of CMV retinitis in them. Thus CD4 count is thought to be strong predictor for the opportunistic infections to arise [7-9].

On clinical examination, majority of the patients showed with only posterior uveitis (86%), remaining 14% had pan uveitis, of which 12% had KPs, flare in anterior chamber and posterior synechiae. 1% had total cataractous lens in one eye and 1% had posterior sub capsular cataract in both eyes. It is proven that the risk of cataract is high when there is considerable long standing inflammatory reaction in anterior chamber, large CMV retinitis lesion, and increased age [6]. In our study cataract was not associated with either of these factors, it might be due to inflammation due to immune recovery after HAART therapy [11,12].

Majority of the patients had multiple large confluent necrosed active retinitis lesion with overlying superficial retinal haemorrhages in periphery threatening the posterior pole. Only two patients presented with only isolated single lesion involving the macula [13,14].

Some of the patients presented with systemic manifestations like skin rashes, high pyrexia due to septicaemia and altered sensorium due to neurological problems. Intravitreal Gangcyclovir 500 to 2000 micro grams, was given to the patients, based upon the site of lesion, size of lesion and involvement of one or both eyes. Gangcyclovir is anti viral drug that is effectual against cytomegalo virus and can be given systemically and also by intra vitreal route, with the former route has advantage of reduced risk of other eye involvement and disadvantage of drug toxicity and haematotoxic effects like neutropenia [8]. In our study systemic therapy was not initiated due to cost factor and also keeping the risk of toxicity in mind [15].

Intravitreal route offers the advantage of providing highest concentration of drug to the retina, without any side effects and drug toxicity. Hence we preferred this route. Initially all the patients were given Intravitreal Gangcyclovir twice a week for 3 to 4 weeks, later on small doses weekly once as maintenance dose. However intravitreal route has risk of endophthalmitis and retinal detachment. We found only one case with retinal detachment on the next day of injection, which might be due to the vitreous traction along the injection site on retina or pre existing necrotic holes. In three patients inflammatory reaction was seen after four injections which might be due to due to immune recovery [3,7]. In these patients injections were stopped and patients treated with topical steroids, and if needed posterior sub tenon steroid was given [12].

Three patients died within few days may due to the poor general health condition. Even after multiple intra vitreal injections few patients did not showed significant improvement. Hence, alternate drugs should be considered.

Conclusion

Majority of the patients in our study presented at the end stage of disease with poor general conditions. Hence early detection of this dreadful disease by screening at the HARRT centres will help to identify these patients and treat them as early as possible to prevent blindness. We can avoid opportunistic infections by maintaining the immune status by initiating HARRT therapy. Also regular ophthalmic checkups and CD4 count evaluation should be advised to these patients. In patients with atypical clinical presentation and lowered CD4 count, PCR should be considered in diagnosing the disease.

Even though our study has limitations like limited sample and alternate drugs not being tested, we could see improvement to the therapy mainly in younger patients between 25 to 35 years. We recommend ophthalmic screening at HARRT centres to prevent blindness in these patients who present late.

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