

Original Research Article

Ocular manifestations of snake bites in a tertiary care hospital in rural Northern Kerala, India

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ABSTRACT

Background: Snake bite is a neglected public health problem worldwide especially in the tropics. Studies on ocular manifestations are still fragmentary. The objective of the study was to find ocular manifestations among the snake bite cases with systemic envenomation admitted in the intensive care units in a tertiary care hospital in rural North Kerala, India during a period of 4 years from May 2012 to May 2016.

Methods: It was a prospective, observational, cross sectional study. Institutional ethical committee approval was obtained for the study. A descriptive analysis of snake bite cases with systemic envenomation was done. Other snake bites are excluded from the study. Patients who needed ophthalmological opinion for ocular symptoms were analyzed.

Results: Total suspected snake bites admitted in ICUs during the study period were 638. Only 7 patients (1%) with haematotoxic envenomation needed ophthalmological opinion for ocular symptoms. Patients in the present study ranged between the age of 11 and 53. Ocular lesions diagnosed among the 6 patients who developed capillary leak syndrome, were bilateral angle closure glaucoma in 3 patients, pan uveitis, disc edema and retinal haemorrhages in 2 patients, bilateral macular oedema. Youngest patient had intracranial haemorrhage and bilateral orbital hemorrhage, leading to exposure keratitis. SAV was administered in all patients ranging from 11-30 vials. All the patients except the patient with orbital haemorrhage had a grave prognosis. Still only one of these patients expired on day 3, rest all patients had better vision and survived due to timely management.

Conclusions: A timely intervention especially at the initial presentation of capillary leak syndrome, can decrease the morbidity and save the life of a patient.

Keywords: Bilateral angle closure glaucoma, Capillary leak syndrome, Disc oedema, Haematotoxic bites, Macular oedema, Orbital haemorrhage, Pan uveitis, Periorbital oedema, Renal failure, Retinal haemorrhages

INTRODUCTION

Snake bite is a neglected public health problem worldwide especially in the tropics as it affects the poor illiterate farmers. Studies on ocular manifestation of snakebite are still fragmentary. The objective of the study was to find ocular manifestations among the snake bite cases admitted in the intensive care units with systemic envenomation in a tertiary care hospital in rural North Kerala, India during a period of 4 years from May 2012 to May 2016.

METHODS

It was a prospective, observational, cross sectional study. Institutional ethical committee approval was obtained for the study. A descriptive analysis of snake bite cases with systemic envenomation during the 4 years admitted in the intensive care units of a tertiary care hospital in rural North Kerala, India was done. Other snake bites were excluded from the study. Patients who needed ophthalmological opinion for ocular symptoms were analyzed in detail. The type of snake and site and time of

bite were noted. Distribution of cases per year was also noted. Hematological and biochemical analysis of blood in view of snake bite and its complications were done. Haematotoxic envenomation was diagnosed from the history of snake bite, identification of snake if possible, the 20 minutes whole blood clotting test and other coagulation profile.

The different systems involved during the course of disease were also noted and timely referral to the concerned specialty was done. Assessment of the severity of envenomation¹ was done, depending on which lyophilized polyvalent enzyme refined equine immunoglobulin (Snake Venom Anti serum. I.P-SAV) was administered. Any untoward side effects of SAV were also noted. The systemic management given to the patients were noted.

Bed side ophthalmological evaluation was done initially as the patients were not ambulant. Visual acuity, gross colour vision, ocular position, extraocular movements, and, anterior segment evaluation were done. IOP was recorded using Schiottz tonometer. Fundus examination was done after dilating with tropicamide eye drops 0.5% when possible after physician's approval. Appropriate treatment was initiated, response to it was noted.

Later when patient was fit to mobilize, detailed evaluation was done in ophthalmology outpatient department. Ocular morbidity if any, were also recorded. Treatment started according to the ocular condition. Response to treatment and the residual ocular morbidity were recorded.

RESULTS

Total suspected snake bites admitted in ICUs during the study period were 638. Year wise distribution of the patients during the study period was as in Table 1.

Table 1: Year wise distribution of the patients during the study period.

Month and year	No. of patients
May 2012- May 2013	119
June 2013- December 2013	106
January 2014- December 2014	145
January 2015- December 2015	127
January 2016- May 2016	141
Total	638

All the 7 patients (1%) referred for ophthalmology evaluation were detected to have haematotoxic envenomation by clinical manifestations and the lab investigations. There were 4 patients with moderate envenomation and 3 patients with severe systemic envenomation. Local reactions were noted in all them and regional lymphadenopathy in 4 of them. 3 of them had respiratory distress and needed ventilator support. All 7 patients except a young patient had capillary leak syndrome and renal involvement which was diagnosed by nephrologist and needed heparin free hemofiltration. Table 2 shows type of snake, severity of envenomation, association of capillary leak and renal failure, ocular diagnosis, visual acuity at presentation and follow up of patients.

Table 2: Case study.

Age	Sex	Snake	Severity of envenomation	Capillary leak	Renal failure	Day of presentation	Ocular Diagnosis	Va at presentation Ou	Va Follow up Ou
11	M	Viper	Moderate	-	-	Day 1- 5 hour	OH, EK ou	CF 3 m	6/6
35	M	-	Moderate	+ chemosis	+	Day 1	ACG ou	CF 1 m	6/18
55	M	Pit viper	Severe	+ chemosis	+	Day 1	ACG ou, DE, RH	CF3 m	Worsened, expired
14	M	-	Moderate	+ chemosis	+	Day 1	ACG ou	CF>3 m	6/6
32	M	-	Severe	+ chemosis	+	Day 2	PU, DE, RH ou	CF 2m	6/18
23	M	Viper	Moderate	+ chemosis	+	Day 1	ME ou	CF 3m	No follow up
36	M	Viper	Severe	+, no chemosis	+	Day 1	DE ou	6/6	No follow up

OH-orbital haemorrhage, EK- exposure Keratitis, ACG –angle closure glaucoma, PU-panuveitis, DE-disc edema, ME –macular edema, RH- retinal haemorrhages, Ou- both eye.



Figure 1: Patient with pan uveitis and hypotony with capillary leak syndrome.

Ocular symptoms were noted in 6 patients on day 1, 1 patient on day 2 of the bite as blurring of vision. 5 patients with capillary leak syndrome presented as facial puffiness, periorbital edema, lid edema and chemosis and blurring. 3 among them developed bilateral angle closure glaucoma later. Among these patients, sub conjunctival haemorrhage was seen in only 1 patient. Visual acuity recorded at bed side in all of them were less than 6/60. 2 of them had mild haziness of cornea with mid dilated fixed pupil.

Yet another patient with capillary leak syndrome and renal failure had bilateral macular oedema. Disc edema was seen in another patient with mild blurring of vision and capillary leak syndrome and facial puffiness, but without chemosis, periorbital and lid edema.

Youngest patient, 5 hours after the bite developed bilateral proptosis which slowly increased causing inferior exposure keratopathy. He developed seizures and CT Scan revealed haemorrhagic infarct of the right frontal lobe along with bilateral intra orbital haemorrhage and bleed into the frontal and ethmoidal sinuses.

SAV was administered in all patients ranging from 11-30 vials. Anaphylactic reactions were not noticed in the study population, so also serum sickness. As and when necessary, relevant referrals were done during management. Heparin free hemofiltration and ventilator support were given when needed. For capillary leak syndrome, nephrologist advised systemic low dose methyl prednisolone at a dose of 125mg/ kg body weight 8 hourly intravenously and hemofiltration for renal failure.

In patients diagnosed to have angle closure glaucoma, IOP was lowered using hyper osmotic agents and topical anti glaucoma medications. Topical steroids hourly was given for the eyes. IOP were controlled. Vision improved in 2 patients. But the oldest patient with pit viper bite, diabetes and hypertension, had angle closure glaucoma, disc edema and retinal haemorrhages. He expired due to acute respiratory distress. Patient with pan uveitis was also treated injection methyl prednisolone 1mg/kg body weight under the cover of potent systemic antibiotics with IOP lowering medications and topical steroids were given

for him. Vision improved from 2/60 to 6/18 in both eyes. Patient survived all the multisystem involvement, except for the local infection at the bite site. Orbital haemorrhage was evacuated by aspiration with wide bore cannula, done after a week. Exposure keratopathy was treated with copious lubricants and cover and patient regained normal vision.

All the patients except the patient with orbital haemorrhage had acute renal failure and capillary leak syndrome which has a grave prognosis. Still only one of the patient with pit viper bite expired on day 3, rest of the patients had better vision and survived.

DISCUSSION

The rural set up in our study population might be the reason for higher incidence which was also reported earlier.² Incidence in present study shows a distinct seasonal pattern with a higher frequency during rains as in the previous studies, when the reptiles come out of their shelters.³ Age of the patients in our study ranged from 11- 53 years and all of them were males. Snakebite is observed in all age groups and more in males probably of their outside nature of work.^{2,4} Most bites were in the evenings and night as in other studies.^{2,5} Most bites were in lower limb, same as with other studies.²

Every bite does not result in complete envenomation and more than half the victims escape without serious poisoning. The effect of snake bite can be classified into vasculotoxic, neuro toxic and myotoxic. Morbidity and mortality due to different species of snake varies and depend on the estimated fatal dose of venom.

Among the 683 patients in our ICUs during 4 years only 1% had ocular symptoms and that too all of them had haematotoxic manifestations. Among the 7 patients they could identify the snake as viper in two and as pit viper in another. Chavan WM and Chavan KD in their report from rural Maharashtra, India on ocular manifestations in patients with snake bite also had reported 6% snake bites as of viper.⁶ Six patients with ocular symptoms had capillary leak syndrome. Suchithra N et al from Kottayam, South Kerala, India had reported on snake bite envenoming with capillary leak syndrome and also acute renal failure but nothing was specified about the ocular involvement in their study group. Capillary leak syndrome is characterised by hypotension, hypoalbuminemia, and hemoconcentration with other features like generalised edema, ascites, encephalopathy, oliguria, compartment syndrome, ischemic end organ damage.⁷ All our patients except 11 year old boy developed renal failure. Kulkarni and Anees observed that only nine (1.4%) children in their study developed acute renal failure, and were all managed conservatively.⁴ Lahori et al in their study of children with snake bites observed only 1% incidence of renal failure, whereas Saini et al reported 4% in their study on adults with snake bites.^{5,8} It could be possible that children have less

chances of developing acute renal failure than adults, following snake bite.⁴

Ocular manifestations are rare after snake bite. Sub conjunctival haemorrhage was noticed in our 2 patients, could be due to haematotoxicity.⁹ 2 of the patients with angle closure glaucoma had mild haziness of cornea with mid dilated fixed pupil probably due to the raised intra ocular pressure. Kumar et al also described a similar condition.⁹

We had 3 cases of bilateral angle closure glaucoma. Interestingly all the 5 reports of similar cases including our report are from South India, of which one is from the same district confirms the geographic predilection of different snakes types.¹⁰⁻¹⁵ All of the patients in this study group had been diagnosed as hematotoxic snake bites and had capillary leak syndrome with acute renal failure which needed heparin free hemofiltration unlike other reports.¹⁵ Chavan WM and Chavan KD in their study on ocular manifestations from Western Maharashtra, India had not mentioned of angle closure glaucoma.⁶ 32 year old young man in present study with acute respiratory distress syndrome, capillary leak syndrome, acute tubular necrosis, acute myocarditis, disseminated intra vascular coagulopathy, toxic acute myocarditis, acute adrenocortical insufficiency and lateral compartment syndrome was diagnosed to have pan uveitis with disc oedema and haemorrhages and hypotony. Patient survived all these due to timely and appropriate intervention except for the cost of treatment.

Acute bilateral angle closure glaucoma has been diagnosed frequently by an idiosyncratic reaction to an inciting pharmacological agent. This form of secondary angle closure glaucoma is due to ciliochoroidal effusion that causes angle closure from forward rotation of lens iris diaphragm and the shallowing of anterior chamber as in our cases too. This is opposed to the pupillary block mechanism seen in patients with anatomically narrow angle. Preethi et al postulated that antihemostatic factors present in viper venom lead to acute fibrinogenolysis, reduction of platelet levels and damage to the vascular endothelium. This could lead to break down of blood aqueous barrier which in turn leads to the edema and extravasation of ciliary body. The mechanism of capillary leak in snake bite is also hypothesised as an increased capillary permeability allowing the fluid and protein to readily pass through the endothelial barrier and to the interstitium.¹⁴ Shiva Prasad C et al found that nearly half of the patients who required haemodialysis following snake bite showed an increase in IOP. Raised IOP in such cases may be explained by the damage to the capillary endothelium leading to edema of the ciliary body.¹¹

A case report by Davenport RC and Budden FH, described optic atrophy following hemotoxic snake bite. They hypothesised retinal ischemia following capillary endothelial damage to be the cause.¹⁶ We would like to stress the importance of raised IOP as a cause of retinal

ganglion cell damage. Olcaysu OO et al et al described about unilateral optic neuritis and angle-closure glaucoma as a result of snake envenomation approximately 18 hours after envenomation, which was treated with good results similar to our study.¹⁷

Buttes JP et al. had reported on uveitis after snake bite.¹⁸ A similar case of anterior uveitis and optic disc edema following haematotoxic bite reported from South India was considered as an adverse effect of SAV or a direct toxic effect of the venom.¹⁹ Their patient was treated with steroids and intra venous methyl prednisolone with visual improvement and resolution of disc edema. S Nayak et al had reported on uveitis following SAV in 2 patients. Both their patients developed severe uveitis 10-15 days following snakebite unlike present study which started on day 2. According to them, the late onset of uveitis excludes the direct effects of the snake toxins on its pathogenesis. Vitritis was probably an immune response to ASV sera. The response to systemic steroids also favours an immune response as the pathogenic mechanism for this uveitis.²⁰ In present study, the fibrinoid anterior uveitis, hypotony and vitritis developed within 4 days unlike in S Nayak et al.

Hyphaema and ghost cell glaucoma though reported were not seen among our patients.²¹

Interestingly all our 7 patients had received SAV ranging from 11-40 vials. S Singh et al state that nonrecognition of discovery of hump nosed pit viper and other species of snakes have led the ASV manufacturers to produce antivenom only against these four species only. They advocate the need to abandon the old concept of “the big four” in order to determine all the medically significant species in India.²²

Jayanta Dutta described a case that developed bilateral retinal haemorrhage following Indian Russell viper (*Daboia russelii*) snakebite.²³ 2 of our patients had flame shaped retinal haemorrhages. Macular edema was noticed in one of our patients with moderate envenomation. Macular infarction due to a viperine bite was reported earlier also.²⁴ The likely cause of visual loss they explained were ophthalmic artery occlusion with subsequent dislodgement of fibrin emboli into the end arterioles at the posterior pole; or retinal necrosis and macular infarction secondary to an aborted DIC process associated with toxic optic neuropathy (venom or ASV serum toxicity). Central retinal artery occlusion though reported earlier by many others was not seen in present study.²⁵⁻²⁷ Bilateral disc edema and retinal haemorrhages were noted in 2 of our patients with severe envenomation.

Case reports of optic nerve involvement are in plenty. First report on optic neuritis following snake bite was in 1953, of a viper bite by Davenport and Budden.¹⁶ Similarly in 1956 Guttman and Friedmann described about a young man who developed bilateral optic neuritis 6 days after receiving a viperine snake-bite in the leg.²⁸

The possible causes of optic neuritis following snake bite have been postulated to be snake venom, allergy to ASV, extensive haemorrhages and capillary damage.²⁸⁻³⁰ There is indirect evidence for each theory. Menon et al have reported cases on optic neuritis, but due to cobra bite.³¹

Mustapha SK et al has reported on bilateral blindness following a carpet viper bite.³² C J Subasinghe et al report the case of a Sri Lankan lady who presented with bilateral blindness secondary to a bilateral posterior circulation ischemic stroke instead of the usual neurological manifestations of Russell's viper envenomation.³³

Kumar et al has reported on a case of exudative retinal detachment following snake bite, the mechanism of which is still unexplained.⁹ BM Rao had reported on a case of bilateral vitreous haemorrhage following a snake bite probably viper.³⁴ M Iqbal had described about a case of endogenous endophthalmitis in a patient with snake bite which was haematotoxic.³⁵

Youngest of our patients developed bilateral proptosis due to orbital haemorrhage and intra cranial haemorrhage. R Naik has reported on a case of orbital cellulitis and pyogenic meningitis following snake bite.³⁶

Altogether the snake bite seems to be a dreaded condition. Fortunately, most of the bites does not cause complete envenomation, so most of the victims escape from death as proven by present study. Capillary leak syndrome and renal failure has a grave prognosis but due to the early identification and timely intervention, present cases had better survival. Most ocular manifestations occurred during 2012-2013. An early detection of the complications in snake bite cases may be a reason for the decreased incidence in the later period of the study, or there is a correlation with the SAV which was administered during that time period.

More, studies are to be conducted to determine the exact etiology and pathogenetic mechanisms of various ocular manifestations of snake bite. Vision threatening complications are even reversible if timely treatment is given, some of them give us clue to the progression of the disease process. Even though ASV remains the mainstay of treatment for snake bite, it is not free of adverse effects, and the treating physician needs to be aware of these rare complications of snake bite and ASV therapy. Role of antsnake venom in ocular complications need to be evaluated. A larger population based study may reveal a clear picture in the pathogenesis of snake bite induced glaucoma and uveitis.

CONCLUSION

Although a major public health problem in many countries, the study of snake bite is still rudimentary. The deficiencies of snake bite management are multifactorial. It requires a joint collaborative efforts from clinicians, researchers, anti-venom manufacturers,

policy makers, public health authorities and international fund raisers to tackle this problem. As far as we clinicians are concerned, an ophthalmology referral is recommended in cases of hemotoxic snake bites in particular, for those with periorbital edema because a timely intervention especially at the initial presentation of capillary leak syndrome can decrease the morbidity and save the life of a patient.

Drawbacks

Ocular examination was not done in all snake bite patients. All our patients were systemically unstable in ICU, so a thorough ophthalmological evaluation and investigations were not possible. Ultra sound biomicroscopy would have been confirmatory in cases with angle closure. The present study also could not ascertain whether snake venom or the ASV was the causative factor for the various ocular manifestations seen in other case series.

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