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CLINICAL CASE REPORT

Visual loss with inner retinal dysfunction, after snake bite: two case reports

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Abstract
Purpose To report two cases of visual loss following snake bite.
Method Retrospective review of medical records including history, examination finding, fundus details and investigation reports (visual field, electroretinogram, visual evoked potential and optical coherence tomogram) at two centers.
Result Two cases of snake bite presented to us with reduction of vision at 1 and 3 months after the incident. The subnormal b wave and abnormal pattern electroretinography in one case pointed at inner retinal dysfunction and neurotoxicity as the cause of visual loss in an apparently normal-looking fundus. The electronegative b wave in the other gave us a clue that the optic atrophy was consecutive (secondary to inner retinal dysfunction due to central retinal artery occlusion).
Conclusion When presented late, diagnosis of visual loss secondary to snake bite becomes difficult and puzzling due to the absence of classical findings. Electrophysiological tests in such cases give us important clue to reach at a definite diagnosis.

Keywords Snake bite · Retinal toxicity · Inner retinal dysfunction · Consecutive optic atrophy · Central retinal artery occlusion

Introduction

Snake bite leading to ophthalmic manifestations is not uncommon. Snake bites are an important and serious medicolegal problem in many parts of the world, especially in South Asian countries. On an average, nearly 200,000 persons fall prey to snake bite per year in India and 35,000–50,000 of them die every year [1]. It can result in vision-threatening complications like optic neuritis [2–6], intraocular hemorrhage, optic atrophy, cataract [7], ghost-cell glaucoma [8], angle-closure glaucoma [9] and very rarely cortical blindness [7]. When presented late, in the absence of classical findings, the diagnosis becomes puzzling. Electrophysiological tests in such cases give us important clues to reach at a definitive etiological diagnosis.

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We report 2 such cases of snake bite (at two different centers of the same institute) who presented to us with reduction of vision at 1 and 3 months after the incident. The subnormal b wave and abnormal pattern electroretinography (ERG) in one case pointed at inner retinal dysfunction and neurotoxicity as the cause of visual loss in an apparently normal-looking fundus. The electronegative b wave in the other gave us a clue that the optic atrophy was consecutive (secondary to inner retinal dysfunction due to central retinal artery occlusion).

Case reports

Case 1

A 26-year-old male presented with complaints of sudden decrease in vision in both the eyes following snake bite to the right foot a month ago. The patient gave history of receiving some oral native, traditional medication by a local doctor in his village after about 2 h of the snake bite. He reportedly had heaviness in the head and eyes for which he received some topical ointment in his eyes. His systemic condition was stable. The details of any antivenom injections given as primary aid were not available with the patient. He noticed visual loss in both eyes that was maximum by third day of the accident and had not changed much since then. On examination, the best-corrected visual acuity in both eyes was 20/80 and the intraocular pressures were 8 mm Hg. Pupillary reactions were normal and there was no relative afferent pupillary defect. Rest of the anterior segment examination was unremarkable in both eyes. The posterior segment examination was also unremarkable in both eyes (Fig. 1a, b). The color vision as tested by Ishihara color plates was normal in both eyes.

A diagnosis of bilateral retrobulbar neuritis was suspected. The patient underwent Humphrey's visual field testing which revealed bilateral diffuse and severe peripheral field loss and dense paracentral scotoma in the nasal hemifield of the right eye (Fig. 2a, b). The pattern visual evoked potential (VEP) was normal in both eyes with normal amplitudes and implicit time (Fig. 3). As the visual fields and VEP did not correlate with the clinical findings, a neurophthalmologist's evaluation was requested who ordered a magnetic resonance imaging (MRI) of brain to rule out any cortical lesions. The MRI scan was normal. The patient was then referred to retina services where a full-field flash electroretinography (ERG) to rule out generalized retinal pathology and pattern ERG (PERG) to look for macular pathology were advised.

The pattern ERG revealed bilaterally decreased amplitude of N95 wave with normal P50 amplitudes, suggesting ganglion cell layer dysfunction (Fig. 4a). The flash ERG (Fig. 4; Table 1) showed subnormal b wave in the dark-adapted 25-db (isolated rod) response (Fig. 4b). The maximal combined response showed a normal a wave with decreased amplitude of b wave suggesting an inner retinal layer dysfunction and normal photoreceptor function (Fig. 4c). The oscillatory potentials (Fig. 4d) were well formed. There was slight reduction in b wave amplitude and normal a wave in the photopic single flash response (Fig. 4e) in both the eyes.

The 30-Hz flicker response showed subnormal a- and b-wave amplitudes (Fig. 4f) in both the eyes. These findings on the ERG suggest an inner retinal layer dysfunction involving mainly the rod pathways with some effect also on the cone pathways and ganglion cells.

Case 2

A 24-year-male presented to us with chief complaints of sudden onset of decreased vision following snake bite 3 month ago. Previous medical record showed that patient was in altered sensorium for 2 days after snake bite. The hematological parameters showed that he had acute 'renal failure and had bleeding diathesis (low hemoglobin, low platelet count, raised serum creatinine and prolonged bleeding and clotting time). He had eight sessions of renal dialysis. At discharge after 3 weeks, his blood parameters including hemoglobin, complete blood count, bleeding and clotting time, blood urea and creatinine had returned to normal limits. He did not have any significant systemic illness in the past. Past medical records of routine eye check up done locally revealed that he had a best-corrected vision of 20/20 and had no other symptoms of low vision or nyctalopia in either eye prior to snake bite.

On examination at our institute, his best-corrected visual acuity was 20/20, N6 in right eye and hand movement close to face in the left eye. The external examination in both eyes was unremarkable except

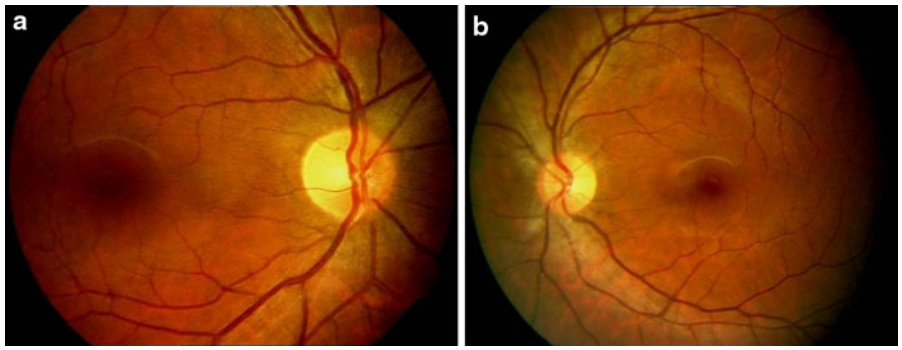

Fig. 1 Fundus picture of the right (**a**) and left eye (**b**)

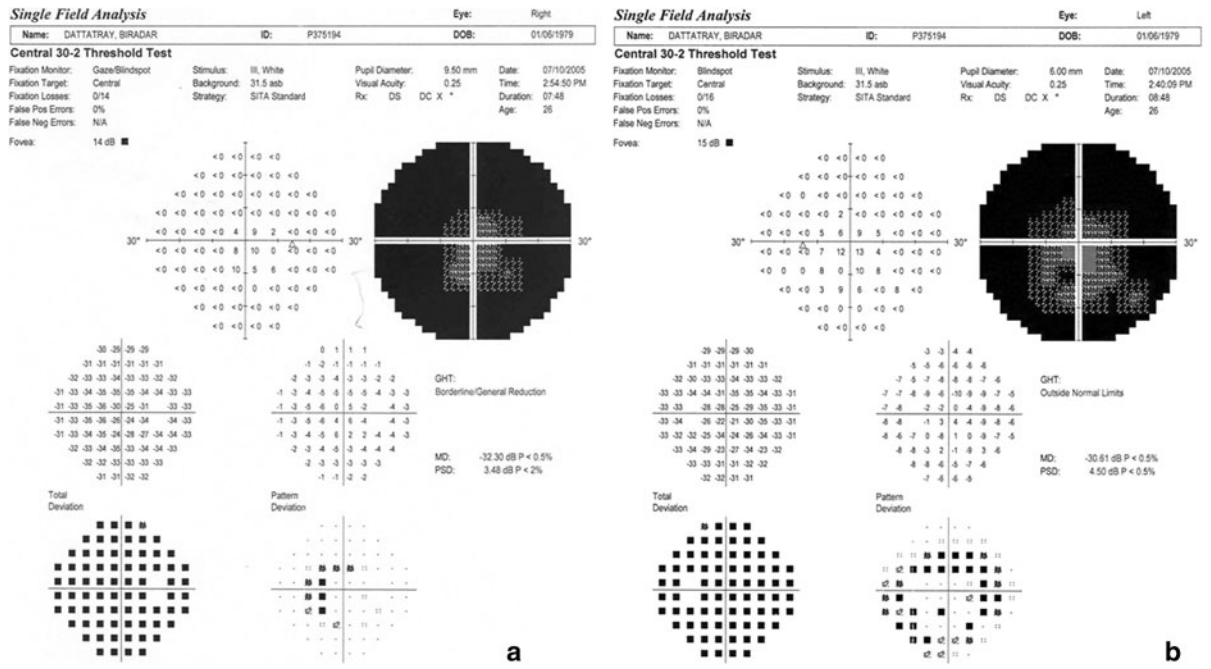

Fig. 2 Visual field (30–2) of right (**a**) and left eye (**b**) showing bilateral diffuse and severe peripheral field loss and dense paracentral scotoma in the nasal hemifield of the right eye

fixed dilated pupil in the left eye. Intraocular pressure was 14 mm of Hg and lens was clear in both eyes. Fundus examination of right eye (Fig. 5a) was within normal limit. Left eye fundus (Fig. 5b) showed clear media, pale optic disc, sclerosis of arterioles and RPE mottling involving the posterior pole and mid-periphery. There were areas of pre-retinal gliosis in macular area. The foveal reflex was absent. Fundus fluorescein angiography of left eye showed areas of transmitted hyperfluorescence due to window defect in macular area. Flash ERG (Fig. 6; Table 2) showed isolated rod response with reduced amplitude in both the eyes. The b-wave amplitude was mildly reduced in the right eye and grossly reduced with electronegative pattern in maximum combined response in the left eye (Fig. 6; Table 1). Photopic responses also showed reduction in b-wave amplitude and prolonged latency (left more than right). Flash VEP (Fig. 7) showed waveforms with decreased amplitude and prolonged latency in the left eye. OCT line scan passing across fovea was suggestive of epiretinal membrane with reduced foveal thickness (central foveal thickness: 92 μ) in the left eye (Fig. 8). Based on the above results, he was diagnosed as a case of consecutive optic atrophy

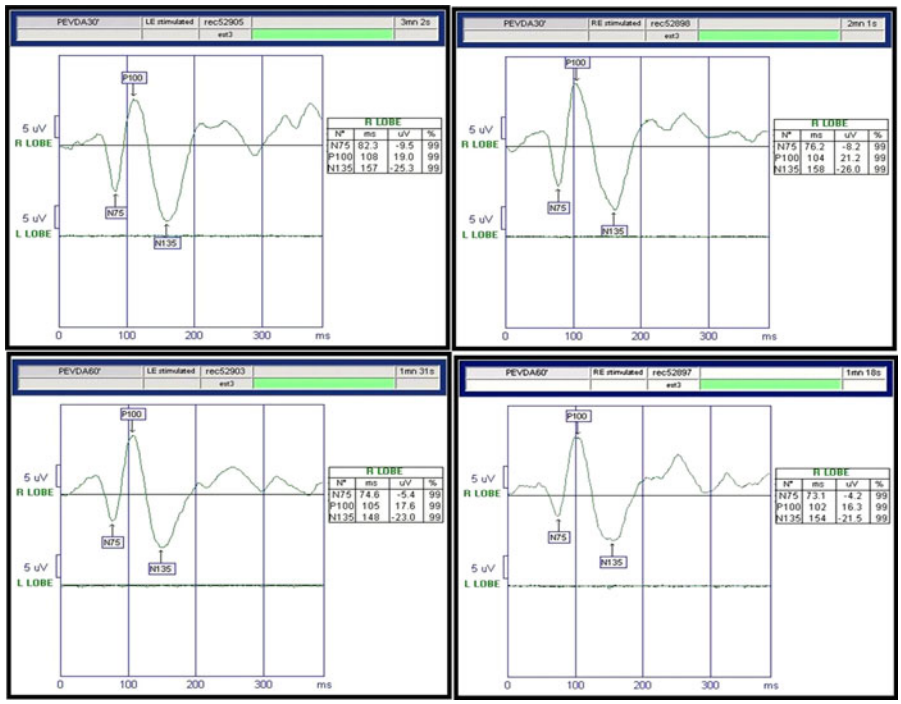

Fig. 3 Pattern visual evoked potential (VEP) in both eyes showing normal amplitudes and implicit time

secondary to resolved central retinal artery occlusion in the left eye.

Discussion

In India, there are 216 species of snakes, of which only four (cobra, krait, Russell's viper and saw-scaled viper) are venomous snakes [1]. Majority of the snake bites (82 %) occur among the rural population [10], who are bitten in agricultural fields while working and also during sleeping outdoors. Most patients are unable to identify the snake species because of either ignorance or poor visibility during darkness. While some snakes (Elapidae, i.e., cobras and krait) are neurotoxic, others such as Viperidae are hemotoxic and vasculotoxic. The venoms of these snakes contain several enzymes and cyclolysin, hematotoxin and neurotoxin. The systemic morbidity and mortality related to snake bite are predominantly due to the neurotoxic effect of the snake venom on the vasomotor center [11]. In our series, the identity of the snake was not known. In case 1, there was no history of hemorrhage and no obvious systemic pathological findings. In case 2, the history and past medical record were suggestive of hemotoxic snake bite with hemolytic anemia with bleeding diathesis leading to end organ failure like acute renal failure and respiratory paralysis.

Visual damage in snake bite is reported to be due to the involvement of the retinal cells, optic nerve or cerebral cortex [11] Retina or optic nerve gets damaged due to direct effect of the venom, or hypersensitivity reaction to antivenin, or extensive hemorrhage and capillary damage [6]. Hypoxic cerebral damage has been believed to be responsible for cortical blindness following snake bite [11] *Electroretinography has not been done in all patients reported in the literature and our cases are possibly the first one to do so.* Previous reports have conducted VEP and no ERG and concluded that the site of lesion is the optic nerve. In the absence of ERG, abnormal VEP does not always suggest optic nerve disease. *Our first patient, we believe for the first time, shows snake venom to cause an inner retinal neuron dysfunction* possibly due to neurotoxicity as there was no clinical or ERG evidence of a vascular pathology in this case. The optic nerve function appeared normal as is evident by clinical examination and VEP. It has been speculated in the past that retinal arterial spasm following snake bite may last long enough to cause complete death of ganglion cells, leading to some atrophy of the inner retina [2]. Singh et al. proposed transient central

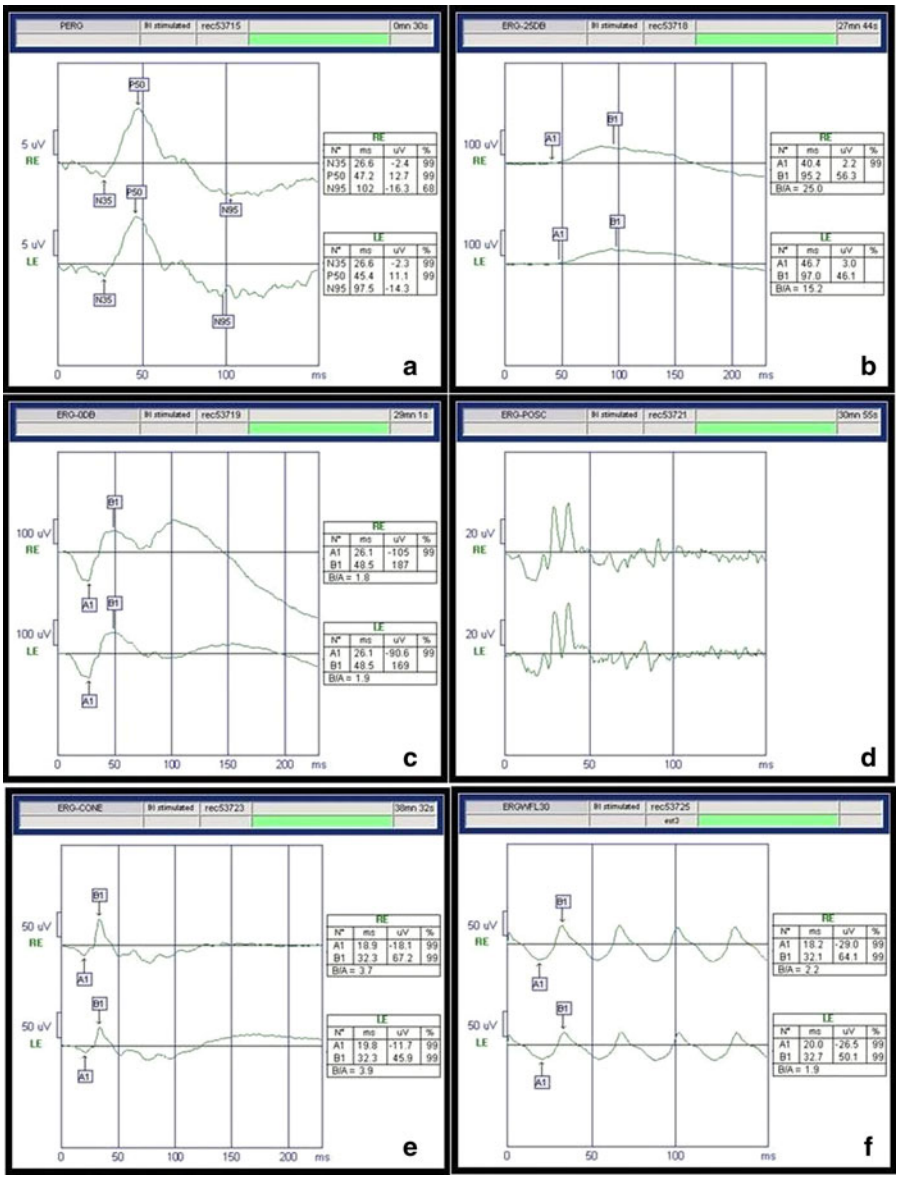

Fig. 4 Pattern and bright flash ERG of both eyes. **a** Pattern ERG showing bilaterally decreased amplitude of N95 wave with normal P50 amplitudes. **b** Dark-adapted 25-db responses showing a subnormal b wave. **c** Maximal combined response showing a normal a wave with decreased amplitude of b wave. **d** Oscillatory potentials showing normal waveforms. **e** and **f** Photopic responses with normal waveforms

retinal artery occlusion caused by a transient embolism in the central retinal artery from disseminated intravascular coagulopathy (DIC), as the cause of visual loss following the snake bite [12]. When the circulation in central retinal artery is restored, the retinal capillaries in the macular region do not refill due to marked ischemic swelling of the retinal ganglion cell layer that leads to compression and occlusion of capillaries in that region. They hypothesized that the inflammation and vasospasm induced by components of the snake venom or anti-snake venom serum, and occlusion of perifoveal capillaries by platelet–fibrin emboli play a key role in causing visual loss after snake bite [13]. A normal fundus examination and normal oscillatory potentials refute any vascular etiology in our patient. Also, there were no systemic or ocular findings suggesting DIC or any other vascular pathology in this case.

Sparing of the optic nerve justifies the extent of visual loss in our patient to be moderate and not severe. Neurotoxicity to the ganglion cells and inner retinal cells seems to be the most likely explanation for

Table 1 Amplitude (μv) and implicit time (ms) of a and b waves in flash ERG in case 1

Flash ERG (metro vision)	Right eye		Left eye		Normal value	
	Amplitude	Implicit time	Amplitude	Implicit time	Amplitude	Implicit time
Isolated rod response	56.3	95.2	46.1	97	157	88
Maximal combined response (a wave)	−105	26.1	−90.6	26.1	−157	24.3
Maximal combined response (b wave)	187	48.5	169	48.5	260	49.4
Oscillatory potentials	Present		Present			
Single cone (a wave)	−18.1	18.9	−11.7	19.8	−23.8	18.9
Single cone (b wave)	67.2	32.3	45.9	32.3	109	34.1
30 Hz flicker (a wave)	−29.0	18.2	−26.5	20.2	−135	18.2
30 Hz flicker (b wave)	64.1	32.1	50.1	32.7	143	33.3

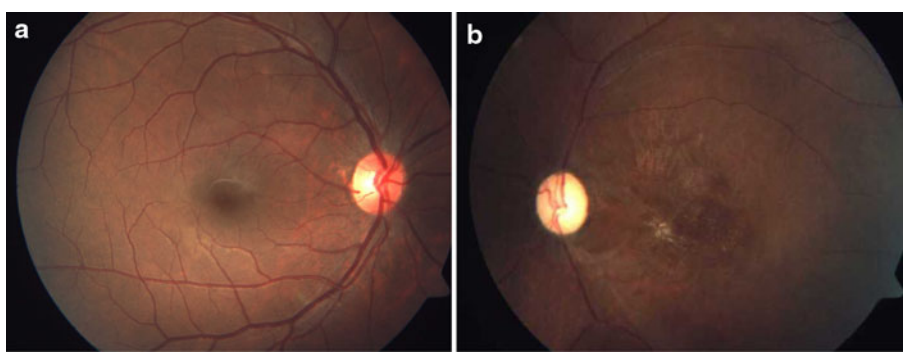

Fig. 5 Fundus picture of right (**a**) and left (**b**) eye. Left eye shows optic disc pallor, arterial attenuation and epiretinal membrane

causing inner retinal layer dysfunction in our patient. Macular photoreceptors seemed largely unaffected. The selective involvement of the rod pathways with relative sparing of cone pathways was seen and needs further basic science evaluation of the effect of venom on retinal cells, for explanation.

The second case probably had disseminated intravascular coagulation with thrombotic occlusion of central retinal artery in the left eye. The CRAO resolved with time leading to consecutive optic atrophy. Electronegative b wave in ERG, arterial sclerosis and diffuse RPE mottling gave us a clue that the patient had acute loss of vision secondary to CRAO in the left eye which later on resolved with consecutive optic atrophy. Interestingly, there was reduction in b-wave (especially rod) amplitude in the

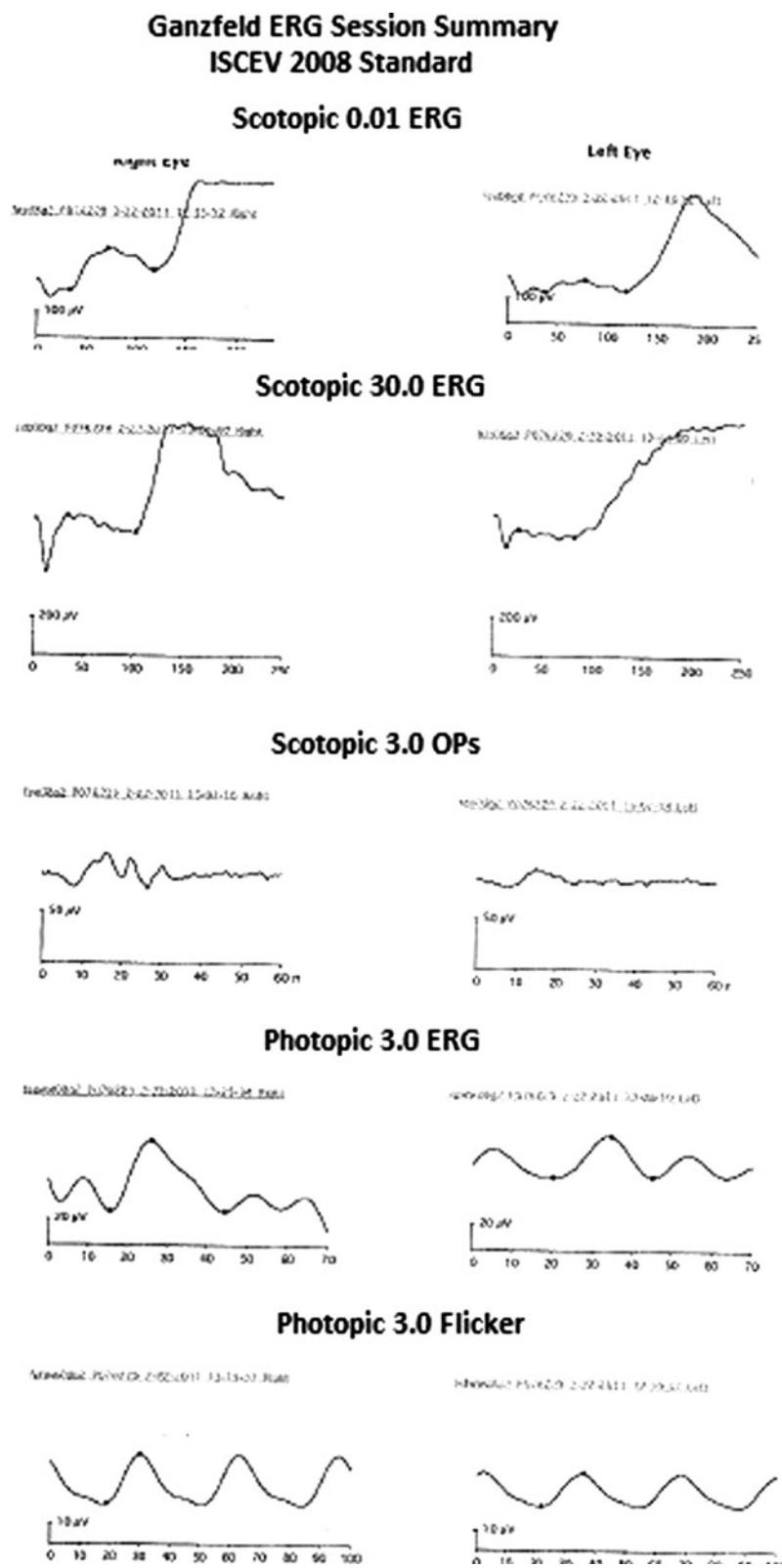

Fig. 6 Bright flash ERG showing normal scotopic responses in both the eyes with electronegative b wave in maximum combined response in left eye

Table 2 Amplitude (μv) and implicit time (ms) of a and b waves in flash ERG in case 2

Flash ERG (Veris science 6.0.10)	Right eye		Left eye		Normal value	
	Amplitude	Implicit time	Amplitude	Implicit time	Amplitude	Implicit time
Isolated rod response	160	65.0	30.0	65.0	225	60.0
Maximal combined response (a wave)	−250	13.0	−140	14.0	−215	17.0
Maximal combined response (b wave)	270	35.0	−55	26.0	404	44.35
Oscillatory potentials	Present		Present			
Single cone (a wave)	−24.0	15.0	−20.0	20.25	−27.4	15.6
Single cone (b wave)	30.0	26.0	15.0	34.75	55.3	27.4
30 Hz flicker (a wave)	−20.00	19	−20.0	22.00	−25.6	16.0
30 Hz flicker (b wave)	14.5	30.00	9.0	36.00	44.4	28.0

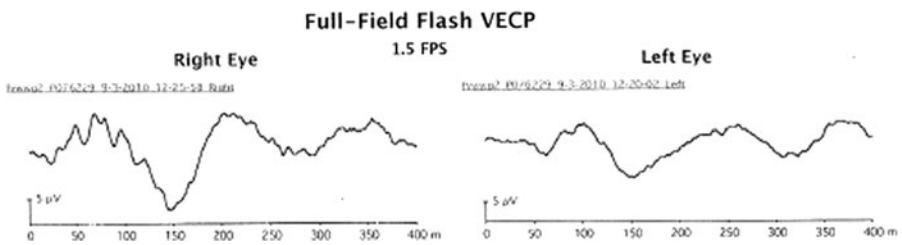

Fig. 7 Flash VEP showing waveforms with decreased amplitude and prolonged latency in left eye

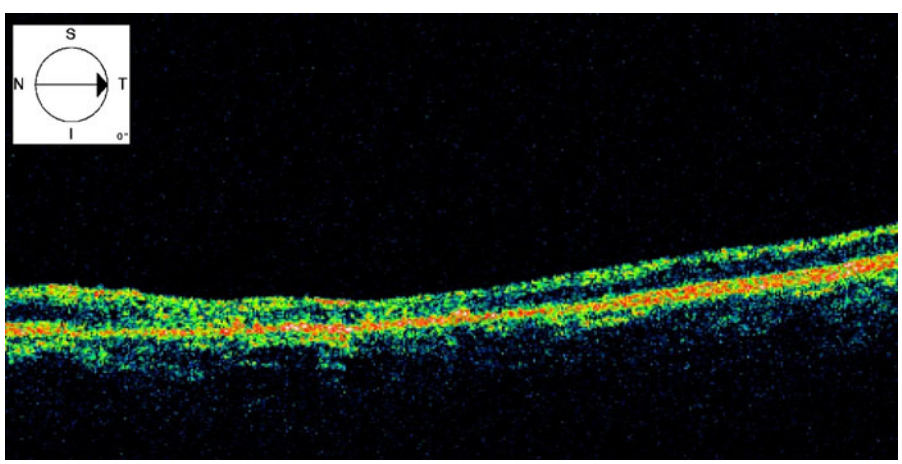

Fig. 8 OCT of the left eye showing epiretinal membrane with reduced foveal thickness (Central foveal thickness: 92 μ) in the left eye

apparently normal right eye indicating some amount of inner retinal dysfunction. This mirrors the finding in case 1 to some extent.

Conclusion

Snake venom can cause moderate to severe visual loss. Moderate visual loss is due to neurotoxicity to retinal cells, while severe loss can be due to a vascular pathology. Not only VEP but flash and macular ERG (pattern or multifocal) should be done to localize the site of insult in such cases. Inner retinal dysfunction of variable extent seen in both the cases raises the possibility that it might be a frequent occurrence after snake bite.

Of course the hypothesis need to be tested in a large series by obtaining ERGs from snake bite victims whether or not they claim visual loss.

Conflict of interest None.

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