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CLINICAL CASE REPORT

Delayed-onset hypoxic cortical blindness: coming back from the abyss

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Abstract
Purpose To report a case of typical delayed-onset hypoxic cortical blindness that occurred few days after resuscitation from drowning in a young male.
Methods Neurological and ophthalmological examination were performed including optical coherence tomography (OCT), Goldmann perimetry, pattern electroretinogram (pERG), pattern and flash visual evoked potentials (pVEP and fVEP) and brain magnetic resonance imaging (MRI).
Results At presentation, at day 12 post-hypoxic incident, best corrected visual acuity (BCVA) was reduced to hand motion OU with an abolished optokinetic nystagmus, a normal fundus and no relative afferent pupillary defect. Macular and peripapillary OCT were normal. Goldmann perimetry revealed bilateral centrocecal scotoma. pERG was normal while pVEPs were undetectable and fVEPs were abnormal with delayed, decreased and disorganized responses, without interhemispheric asymmetry. Brain MRI disclosed a bilateral cortical–subcortical occipital hypersignal with laminar necrosis and thus confirmed the diagnosis of delayed-onset hypoxic cortical blindness. Visual rehabilitation, including visual stimulation in the scotomatous areas, was associated with a dramatic and rapid visual improvement with a BCVA of 20/32 OU, an ability to read after 2 weeks (day 30 post-hypoxic incident), and a reduction in the size of the scotoma.
Conclusion Delayed-onset hypoxic cortical blindness is a rare presentation of cortical blindness that develops few days after a cerebral hypoxic stress. While initial presentation can be catastrophic, visual

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improvement may be spectacular and enhanced with visual rehabilitation.

Keywords Cortical blindness · Apnea · Visual evoked potential · Visual rehabilitation

Introduction

Cortical blindness (CB) is caused by damage to the primary visual cortex. Hypoxemia or stroke involving the posterior or middle cerebral arteries accounts for the great majority of cases. Traumatic brain injury, tumors or their resection and even congenital conditions may result in similar presentation [1]. CB is a well-recognized complication of hypoxic-ischemic encephalopathy (HIE), which follows cardiac arrest and/or deep and prolonged hypoxemia. It usually appears immediately on recovering consciousness after resuscitation [2]. However, the onset of CB or other neurological complications may be delayed for days or weeks after anoxic exposure [3]. We present here a case of a young male with delayed-onset hypoxic CB, which occurred one week after drowning resuscitation, with spectacular visual recovery following visual rehabilitation.

Case presentation

An 18-year-old Tahitian boy felt unconscious while freediving at a depth of 30 m, with an estimated hypoxia time of 3 min, without cardiac arrest. The patient was admitted in the intensive care unit (ICU) one hour later, with a Glasgow Coma Score of 3 and a bilateral mydriasis. He was sedated and intubated. Cranial computed tomodensitometry was normal. He was extubated 24 h later. At this moment, the patient did not complain of visual loss. Four days later (day 5 post-hypoxic incident), the patient reported a thunderclap headache that lasted a few hours, with concomitant bilateral visual loss. Best corrected visual acuity (BCVA) was "hand motion" OU with an abolished optokinetic reflex, a normal pupillary light reflex and a normal ocular biomicroscopic examination. Brain CT scan and MRI were considered normal. The patient was referred to our hospital at day 12 post-hypoxic incident for further evaluation. At admission, there was neither visual hallucination, focal deficit nor memory or language disorders. Both peripapillary and macular spectral domain OCT scans were normal. The Goldmann perimetry revealed a bilateral centrocecal scotoma (Fig. 1A, B). Electrophysiological procedures were performed in accordance with the ISCEV standards [4, 5]. Pattern electroretinogram (pERG) was normal (Fig. 2A, B), but visual evoked potentials (VEP) were altered. The monocular and binocular flash VEP (fVEP), performed with a field of 20°, were delayed, decreased in amplitude and simplified responses without interhemispheric asymmetry (Fig. 2C–F). The monocular and binocular pattern VEP (pVEP), performed with large (1°) and small (0.25°) checks, were undiscernible from background noise (Fig. 2G–I). A new brain MRI disclosed bilateral cortical-subcortical occipital hypersignal with laminar necrosis (Fig. 3) and confirmed the diagnosis of delayed-onset hypoxic CB. The patient was referred for visual rehabilitation in a dedicated inpatient facility, where he stayed 2 weeks with daily sessions of visual restoration training (VRT) involving stimulations of the blind visual field using detection and discrimination tasks. It was associated with a spectacular improvement with a BCVA of 20/32 OU and reading ability, and a decrease of the size of the centrocecal scotoma at day 30 post-hypoxic incident (Fig. 1C, D).

The last measures were obtained at this time point, following which the patient returned home (in French Polynesia) where electrophysiological testing is unavailable, and was lost to follow-up.

Discussion

In a patient with sudden bilateral visual loss, CB should be suspected in case of normal fundus, persistence of the pupillary light reflex, the abolition of both the menace blinking response and the optokinetic reflex [6]. Neurological examination may reveal concomitant anosognosia, memory loss or visual hallucinations. Key complimentary exams are normal macular and retinal nerve fiber layer OCT, normal ERG and occipital cortex lesions on MRI. Visual evoked potentials can be normal or altered, as in the present case [7]. Common causes of HIE in adults are cardiac arrest, severe hypotension and drowning. In children common dehydration, neonatal anoxia and

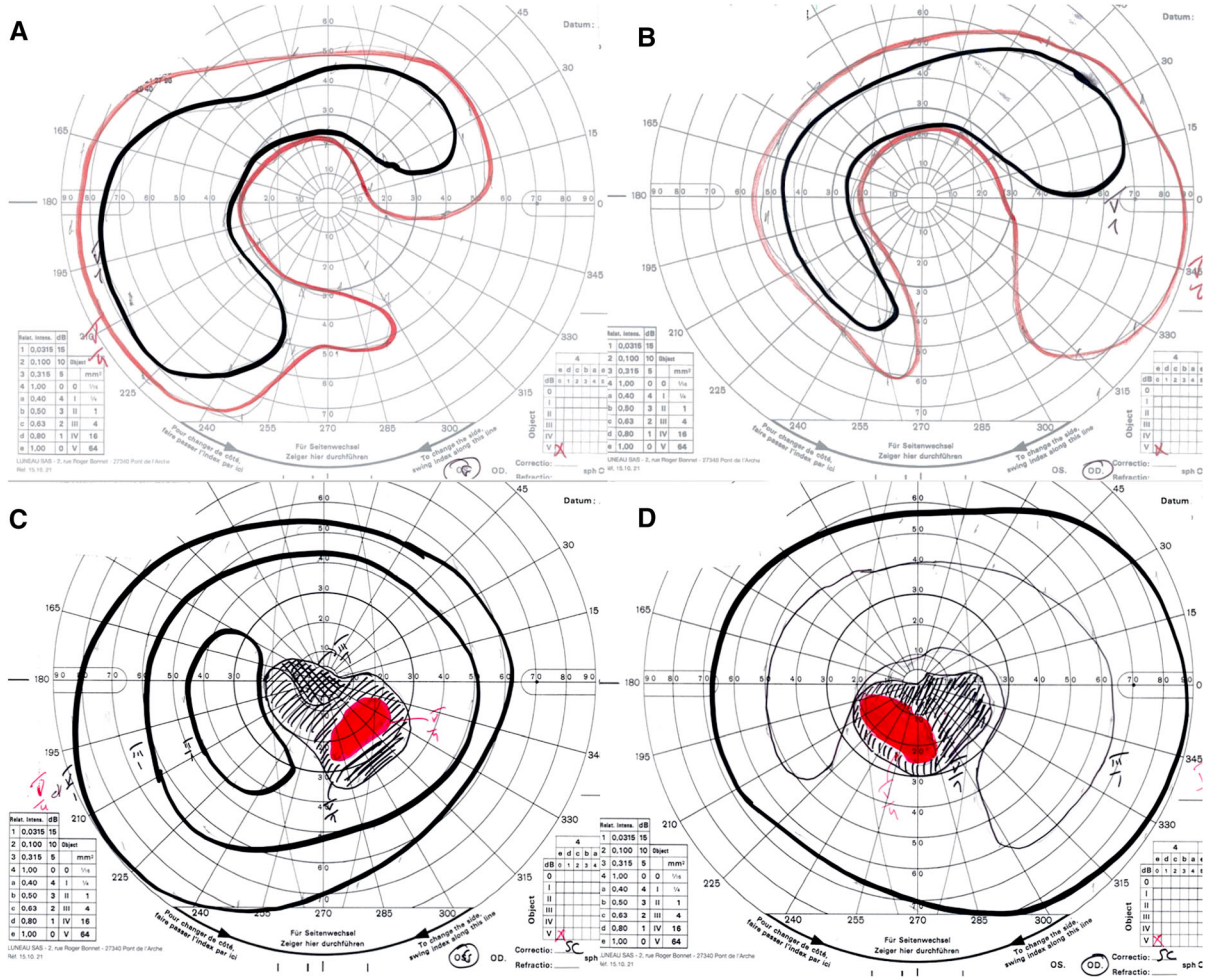
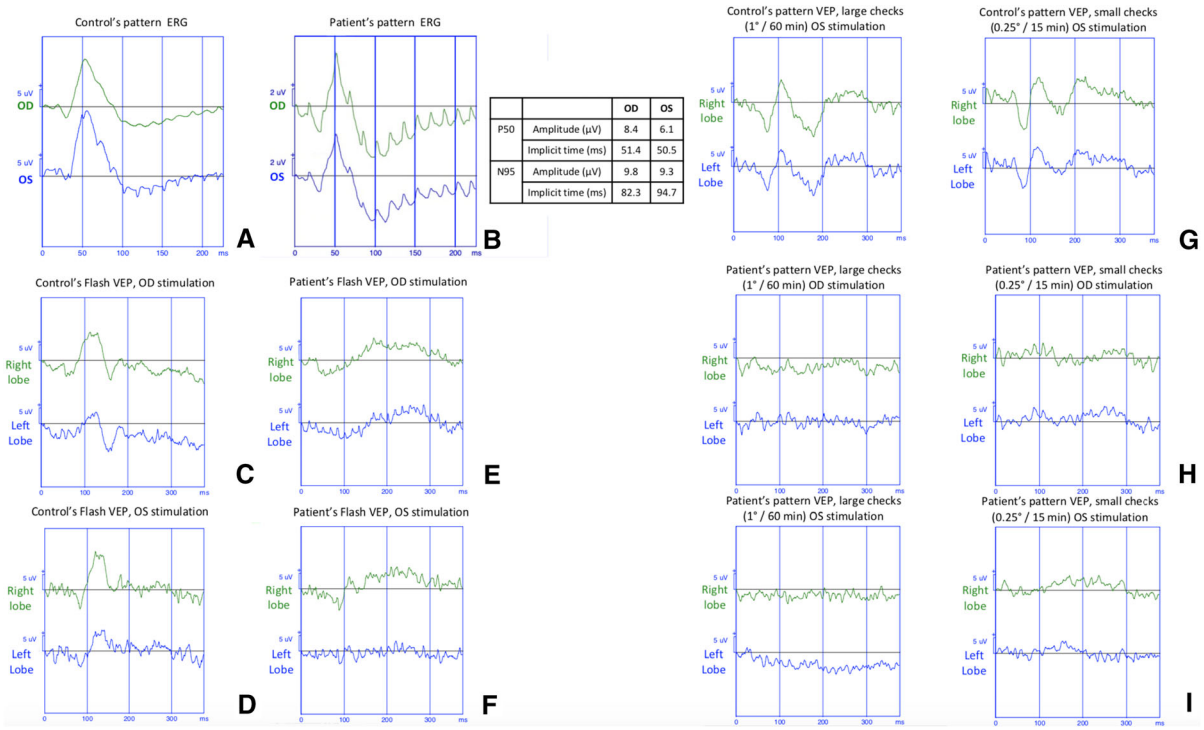


Fig. 1 Goldmann perimetry. **A**, **B** At admission (day 12 post-hypoxic incident): bilateral centrocecal scotoma (red lines indicate the V-4 isopter) **C**, **D** Two weeks after the onset of visual rehabilitation (day 30 post-hypoxic incident): bilateral reduction of the scotomas (red lines indicate the V-4 isopter, red spots indicate scotomas measured with the V-4 target, hatched zones indicate scotoma measured with the V-1 target, and cross-hatched zones indicate additional scotoma measured with the III-1 target)

abusive head trauma may be involved. At any age, the damages predominate in the cerebral cortex, the corpus striatum, the hippocampus and the cerebellum [8]. A recent study showed that the occipital lobe may be an isolated target in HIE with CB as the only clinical manifestation [9]. It is widely recognized that anoxia produces acute neurological deficits. However, severe neurological lesions may be delayed for days or weeks after hypoxic/anoxic incident [3].

Delayed-onset hypoxic CB is a rare but recognized syndrome which critical care physician, neurologist and ophthalmologist should be aware of. It is characterized by a CB with occipital lesions on MRI, occurring few days after a hypoxic/anoxic incident [2, 9–11]. The pathophysiology of delayed-onset CB is poorly understood. Possible mechanisms include cumulative oxidative stress and glutamate excitotoxicity leading to neuronal cell damage [12]. Pathological studies showed that cortical damages were associated lesions in the white matter [3].

Unlike classic hypoxic CB, visual prognosis after delayed-onset hypoxic CB is reportedly good with a significant increase in vision after few weeks, as in our case [2, 8, 10, 11, 13]. In cortical blindness, vision recovery is due to histological normalization of the dysfunctional cortex by resolution of edema or



		OD	OS
P50	Amplitude (μV)	8.4	6.1
	Implicit time (ms)	51.4	50.5
N95	Amplitude (μV)	9.8	9.3
	Implicit time (ms)	82.3	94.7

Fig. 2 Electrophysiological explorations. **A** Pattern electroretinogram (pERG) of an age-matched control and **B** pERG of the patient which is normal. The associated table provides the values for P50 and N95 amplitudes and implicit times for both eyes of the patient. **C**–**F** Flash visual evoked potentials (fVEP). fVEP traces of right (**C**) and left eye (**D**) stimulation of an age-matched control subject. Patient's fVEP traces of right (**E**) and left eye (**F**) stimulation, showing delayed, decreased and disorganized responses, without interhemispheric asymmetry **G**–**I** Monocular pattern VEP (pVEP). **G** pVEP traces of left eye stimulation with large (1°) and small (0.25°) checks of an age-matched control subject. **H**, **I** Patient's pVEP traces of right and left eye stimulation, which are undiscernible from background noise

restitution of axonal connections and functional recovery through the use of minute parts of preserved field, or "nonstriate vision" [6]. Visual hallucinations and perceptual problems may occur during recovery and are the clinical manifestations of the electrophysiological hyperexcitability of the recovering visual cortex [13]. However, visual cognitive, field and visual perceptual deficits may persist for a long time [1]. Although spontaneous recovery usually occurs in delayed-onset hypoxic CB, a quick and strong visual rehabilitation may promote and enhance functional recovery [1, 14]. Nevertheless, there is no standardized protocol for VRT [15] and a recent meta-analysis concluded that there was insufficient evidence to reach generalized conclusions about the benefits of VRT for patients with visual field defects after stroke [16]. Current rehabilitation techniques include stimulation of damaged visual areas and eye movement optimization [1, 14, 17]. Depending on the method, restitution training approaches involve static, moving or flickering target presented either in the center or at the border of the blind field in order to stimulate cerebral plasticity [1]. Infrared eye trackers can be used to enforce fixation during testing [1]. Visual stimulation and visual strategies are associated with cognitive rehabilitation, ideally in ecological situations to stimulate the nervous system in various dimensions being vision, hearing but also sensorimotor and cognitive tasks (verbal instructions) [17]. Stimulating as many neuronal networks as possible in intensity, repetition and amplitude is indeed the ideal rehabilitation scheme [17] that can only be achieved with a multidisciplinary team offering the wide spectrum of skills.

We acknowledge that longer ophthalmological follow-up of the patient would have been of interest, notably to assess potential further improvement in visual acuity and visual field. Besides, in the absence

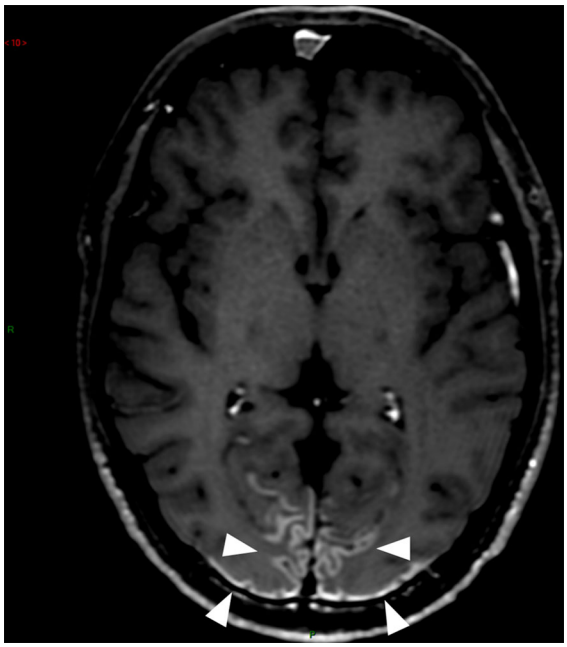


Fig. 3 Contrast enhanced magnetic resonance imaging performed 2 weeks after the accident. 3D T1-weighted Spin Echo sequence showing bilateral occipital cortical hyperintense lesions, consistent with cortical laminar necrosis of the primary visual cortex (arrowheads)

of controlled study, the role of VRT cannot be fully ascertained in this context.

To summarize, clinicians should be aware that post-anoxic cortical blindness can occur few days or weeks after an ischemic incident. While spontaneous recovery usually occurs, intensive visual rehabilitation may enhance functional recovery.

Authors' contributions AM, IA, ML and AR analyzed the data, drafted and revised the manuscript. CG, MDM and PS drafted and revised the manuscript.

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Availability of data and materials All data and material are available in the manuscript.

Declarations

Conflict of interest All authors certify that they have no conflicts of interests in relationship with this paper.

Statement of human rights All procedures performed in this case report were performed in accordance with the ethical standards of Bicetre Paris Scaly University Hospital and with the tenets off the declaration of Helsinki.

Statement on the welfare of animals Not applicable.

Informed consent For this type of study, formal consent is not required.

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