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Hypoxic Encephalopathy

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1. Introduction

Encephalopathy is a broad concept that refers to a syndrome of overall brain dysfunction. Various systemic diseases can provoke encephalopathy, and the prominent related neurological signs and symptoms may mask the underlying disorder. Lack of oxygen and of blood flow to the brain are main causes of this condition. Often both mechanisms are related to heart failure and circulation, and of the lungs and respiration. It is difficult to ascertain which predominates. Hence, physicians use the ambiguous term of cardiorespiratory failure.

Hypoxic/anoxic brain injury can result from insufficient cerebral blood flow, reduced oxygen availability, reduced oxygen carriage by blood, or metabolic interference with the use of available oxygen (Commichau, 2006).

Ischemic - Hypoxic encephalopathy is often seen in emergency departments and can have a disastrous prognosis. A large number of medical conditions can lead to this situation, mainly (Ropper & Brown, 2005):

1. Heart failure followed by respiratory depression secondary to massive blood loss, septic or traumatic shock, and heart disease, such as myocardial infarction or ventricular arrhythmia.
2. Respiratory failure followed by cardiac arrest as a result of low oxygen intake (in tracheal compression or obstruction, drowning, strangulation, aspiration of gastric content, or during general anesthesia if the inspired gas is poor in oxygen), respiratory muscles weakness in neurological diseases (Guillain-Barré syndrome, amyotrophic lateral sclerosis, myasthenia gravis) or central nervous system injury (mainly spinal cord injury).
3. Reduced oxygen carriage by the blood in carbon monoxide poisoning.
4. Histotoxicity in cyanide poisoning.

Physicians should also be aware of the delayed form, a rare condition that is difficult to diagnose. Delayed postanoxic encephalopathy (DPE) should be suspected in patients who have experienced respiratory depression or when a patient presents with subacute onset of cognitive and neuropsychiatric deficits. We describe a case of delayed postanoxic encephalopathy following acute intake of cocaine and heroin.

2. Epidemiology

In industrialized countries, out-of-hospital cardiac arrest occurs in 0.04 to 0.13% of the total population per year (Callans, 2004). Despite advances in prevention and treatment of

cardiac and respiratory failure, the prognosis after a cardiopulmonary arrest remains poor. This condition represents an important cause of death in developed countries. However, due to its high incidence, even with low survival rates, the prevalence of survivors is surprisingly high (Callans, 2004; Young, 2009). Even when cardiac arrests and resuscitation take place in the hospital, fewer than one in five patients survive to discharge (Pederby, 2003). After a severe hypoxic insult, the brain may have become critically injured and patients may remain comatose, leading ultimately to severe cognitive impairment with a fully dependence for the basic life activities or to a vegetative state (Levy et al., 1985; Longstreth et al., 1983). The economical impact of these patients is substantial since their need for long-term care is unavoidable (Gray et al., 1991).

3. Pathophysiology

Brain hypoxia and ischemia due to systemic hypoxemia, reduced cerebral blood flow, or both are the primary physiological processes that lead to hypoxic-ischemic encephalopathy. The brain damage that occurs following hypoxic insult differs depending on the underlying mechanism. Ischemia (low cerebral blood flow) usually results in patchy infarctions in border zones between the major cerebral arteries (Fig. 1), whereas anoxia (reduced oxygen carriage by the blood) provokes neuronal death, mainly in the hippocampus, deep folia of the cerebellum, and cerebral cortex. In extreme cases of hypoxia and ischemia, more generalized damage occurs in the cerebral cortex, deep nuclei, and cerebellum. The deep grey matter of the brainstem is highly resistant to anoxia and tends to survive after relatively severe and prolonged anoxia when extensive cortical damage has been inflicted (Plum & Posner, 1980).

At the cellular level, neuronal injury in hypoxic-ischemic encephalopathy is a progressive process that starts with necrosis in which the magnitude of the final neuronal damage depends on the duration and severity of the initial insult combined to the effects of reperfusion injury, and apoptosis. The necrotic tissue swells rapidly, mainly because of excessive of both intracellular and intercellular water content. Initially, venous blood darkens owing to an increase in reduced hemoglobin. The tissue becomes pale and arteries and arterioles become narrowed, especially in the pale areas. Eventually, during the reperfusion phase, the sequence is reversed and slight hyperemia might be present. Necrosis not only affects neurons but also oligodendroglial cells in the white matter (Lo et al., 2003).

Furthermore, the injury to both neurons and oligodendroglial cells secondary to necrosis is followed by an inflammatory response, activating endothelial cells to secrete proteases and cytokines and to express cell adhesion molecules that attract additional inflammatory cells (Lo et al., 2003).

At the molecular level, ischemia and anoxia lead to malfunction of the essential processes that sustain the Krebs cycle and electron transport system (Singh et al., 1992). In situations of severe, persistent hypoxia, neurons catabolize themselves to maintain activity, tissue necrosis ensues, and there is an accumulation of catabolic products and excitatory neurotransmitters, such as glutamate. Ultimately, massive intracellular influx of calcium leads to diffuse cell destruction (DW Choi & Rothman, 1990).



Fig. 1. Cranial CT after cardiac arrest demonstrating watershed infarction between the anterior and middle and between the middle and posterior cerebral arteries.

After transient recovery of cerebral energy metabolism, a secondary phase of apoptotic neuronal death occurs leading to a delayed injury (Lo et al., 2003). Experimental studies have suggested that delayed apoptosis can be triggered during anoxia, causing demyelination and neuronal death some time after the anoxic insult (Sheth & Bodensteiner, 1998; Kim HY et al., 2002). The physiopathogenic mechanism of delayed lesions remains unclear although two main hypotheses have been proposed: neuronal apoptosis (Sheth & Bodensteiner, 1998; Kim HY et al., 2002) and demyelination (Barker et al., 1999). In DPE, the initial anoxia should be severe enough for a threshold to be exceeded triggering apoptosis, which leads to neuronal death. The demyelination visible in cranial MRI is attributed to oligodendroglial dysfunction and attempts have been made to relate this to an arylsulphatase A deficiency (Gottfried, 1997; Barker et al., 1999).

Carbon monoxide (CO) is an exogenous toxin which produces a unique anoxia frequently associated with delayed neurologic deterioration (Choi IS, 1983). CO possesses a great affinity for hemoglobin (over 200 times that of oxygen) and drastically displaces the oxygen content of blood, leading to prolonged hypoxia and acidosis. Cardiac toxicity and hypotension generally follow and contribute to brain damage. After CO poisoning, two histopathological patterns have been reported in the literature. One pattern comprises degeneration of the cortical laminae and basal ganglia and is supposed to occur short after CO poisoning and the other one entails different degrees of demyelination in the centrum semiovale, occurring in close relation to the delayed form of encephalopathy (Custodio & Bradsford, 2004; Hori et al., 1991).

Cyanide (CN) makes the cells of an organism unable to use oxygen through the inhibition of cytochrome C oxidase affecting primarily the myocardium and secondarily the brain (Beasley et al., 1998).

4. Clinical syndromes

Different clinical syndromes can occur after an anoxia, depending on the severity, the duration and the underlying mechanism of the hypoxic insult. Neurological syndromes occurring after anoxia are summarized in Table 1.

Blood oxygen saturation is used as an objective measurement to predict the severity of cerebral hypoxia: 95-100% saturation is considered normal, 91-94% is considered mild, 86-90% is considered moderate and anything below 86% is considered severe (Butterworth & Roger). It is important, though, that the physician bears in mind that if CO poisoning is suspected, blood oxygen saturation is not reliable and carboxyhemoglobine should be measured.

-
- 1) Mild sustained hypoxia
 - (a) Cognitive impairment
 - (b) Confusional states
 - (c) Delirium
 - 2) Brief anoxic-ischemic events
 - (a) Syncope
 - (b) Abortive or actual generalized seizure activity
 - 3) Sustained severe hypoxia
 - (a) Coma with residual neurological deficits
 1. Dementia
 2. Vegetative state
 3. Brain death
 - (b) Seizure activity
 - (c) Watershed infarction of cerebrum, cerebellum, spinal cord
 - (d) Infarction distal to a pre-existing arterial stenosis or occlusion
 - (e) Postanoxic demyelination
-

Table 1. Clinical syndromes following anoxia (Caronna & Finklestein, 1978).

4.1 Postanoxic coma, sequelae, and clinical prognosis

Because of its autoregulatory capability, the brain can respond to a decrease in oxygen supply by increasing the cerebral blood flow. If this response suffices to maintain the minimum oxygen required, the subject will remain asymptomatic. When this increase is insufficient, symptoms of cerebral hypoxia will gradually develop (Butterworth & Roger). Mild hypoxia results in less severe symptoms, including inattentiveness, difficulties with complex tasks, impaired short-term memory, and motor incoordination. If the oxygen deprivation is prolonged or severe, it can result in loss of consciousness, seizures, deep coma, cessation of brainstem reflexes, and ultimately, brain death (Safar, 1986).

The duration of anoxia necessary to provoke brain damage has not been established (Safar, 1986). There are several potentially important related factors, such as prearrest blood glucose levels, preischemic medication (aspirin and calcium channel blockers), associated hypothermia (Müllner et al., 1998), and age (Kriel et al., 1994). Neurons can tolerate approximately 20 minutes of normothermic ischemic anoxia, but cerebral recovery will be impeded by secondary brain damage after reperfusion. It is generally accepted that more than five minutes of anoxia during circulatory arrest can cause serious brain injury and result in sequelae (Safar, 1986).

After cardiac arrest, postanoxic patients remain in deep coma in which even brainstem function may be absent, and ventilation support becomes necessary. The duration of this state depends on the length of the anoxic insult, but generally, patients regain brainstem function in one to three hours. From the initial flaccidity, patients can develop decerebrate or decorticate posturing before awakening. Awakening is gradual and has different patterns. Patients who awake within 24 hours after cardiac arrest may be agitated and confused for some hours or days until cognitive functioning recovers. Arousal in other patients can take longer, and in the interim they show reflex motor posturing, grasping, eye opening and, finally, arousal. At this time, previously hidden signs secondary to focal or multifocal infarction may appear. Diffuse cortical injury mainly presents as short-term memory loss, inattention, emotional lability, hallucinations, and difficulty in the flow of thoughts, whereas basal ganglia injury manifests as parkinsonian syndrome or chorea. Throughout this process, seizures of any kind can appear (Snyder et al., 1980). Axial myoclonus or asynchronous distal limb myoclonus are common within the first 12 hours after cardiac arrest (Snyder et al., 1980). Generalized tonic-clonic seizures occasionally occur. Partial simple or complex seizures can also develop and be misdiagnosed as a prolongation of the patient's postanoxic stupor or confusional state (Wijdicks, 1995).

The prognosis after anoxic coma is difficult to ascertain, but guidelines have been designed based on a series of 210 patients (Levy et al., 1985) (Table 2).

In a more extensive review of this subject (Wijdicks et al., 2006), the following factors were cited as indicators of a poor prognosis after cardiopulmonary arrest: absent papillary light response or corneal reflexes; absent motor response or extensor response to pain on the third day in observation, and myoclonus status epilepticus. Bilateral absent cortical response on somatosensory evoked potential studies recorded three days after anoxia also indicate a bad prognosis. A burst suppression pattern on electroencephalography (EEG) or generalized epileptiform discharges predicts a poor outcome, but with insufficient prognostic accuracy. Serum neuron-specific enolase above 33 g/L is also predictive of a poor outcome.

Time since cardiac arrest	Patients with virtually no chance of regaining independence	Patients with best chance of regaining independence
Initial examination	No pupillary light reflex in the absence of other causes	Pupillary light reflexes present; motor response decorticate or decerebrate posturing; spontaneous eye movements conjugately roving or orienting
1 day	1-day motor response no better than decorticate posturing; spontaneous eye movements neither orienting nor conjugate; roving	1-day motor response withdrawal or better; 1-day eye opening to noise or spontaneously
3 days	3-day motor response no better than decorticate posturing	Motor response withdrawal or better; spontaneous eye movements normal
1 week	No obeying commands; spontaneous eye movements neither orienting nor conjugate	Obeying commands

Table 2. Guidelines to identify patients with a poor or favorable prognosis after cardiopulmonary arrest (Levy et al., 1985)

4.2 Persistent vegetative state

Some patients who achieve arousal are otherwise unaware of environmental stimuli. This tragic situation is known as persistent vegetative state (previously vegetative coma).

Patients in a vegetative state can present brainstem reflexes and sleep-wake cycles, and achieve certain behavior patterns, such as yawning, smiling, crying, sneezing, or blinking to a threat. The motor responses tend to be decorticated or decerebrate posturing - Non consistent, nonreflexive response to stimulation and following moving objects with gaze can be achieved. If this condition is maintained a month after the resuscitation, it is considered a persistent vegetative state. (American Neurological Association Committee on Ethical Affairs, 1993).

The underlying pathologic substrate of this state is diffuse prosencephalon injury with brainstem preservation. The EEG is, therefore, abnormal and shows a complete absence of cortical alpha activity, although arousal changes can be seen (Commichau, 2006). CT scans may initially show diffuse and multifocal cerebral damage and eventually the development of progressive and severe cerebral atrophy. (American Neurological Association Committee on Ethical Affairs, 1993).

4.3 Cerebral edema

Some, but not all patients who experience cardiopulmonary arrest have subsequent cerebral edema (Fig. 2). This is not accompanied by papilledema, and herniation is uncommon (Commichau, 2006). Autopsy study has shown that edema is more likely to be found in patients with deep coma and prolonged survival, which indicates that it might be a post-necrotic feature rather than a result of inflammation (Commichau, 2006). Intracranial

hypertension may be more likely to develop when the hypoxic insult is due to respiratory failure. Some authors consider that this could be related to the presence of hypercapnia and acidosis previous to the cardiopulmonary arrest, but the value of these parameters as prognostic factors is poor (Müllner, 1997; Müllner 1998).



Fig. 2. Cranial CT without contrast infusion after cardiac arrest demonstrating the loss of distinction between gray and white matter throughout the cerebral hemispheres. The patient remained comatose and became vegetative.

The early presence of high intracranial pressure secondary to cerebral edema after a cardiopulmonary arrest may predict a poor prognosis in relation to the global tissue death (Commichau, 2006). There is no evidence that treatment of this condition with; hyperventilation (ECC, 2005), corticosteroids (Jastremski et al., 1989), osmotic diuretics, barbiturate-induced coma, or ventriculostomy might be effective (Brain Resuscitation Clinical Trial I Study Group, 1986).

4.4 Brain death

Definition of death in the adult can be established in two different situations: 1) when there is an irreversible cessation of cardiopulmonary function and 2) when the irreversible cessation function is that of the central nervous system. Diagnosis in the former group is acquired after clinical examination. In the latter group, patients are supported artificially by mechanical ventilation, then this diagnosis becomes a difficult issue.

The ultimate and most severe consequence of anoxia is brain death, in which there is no cerebral or brainstem activity, patients cannot breathe on their own, and only blood pressure and cardiac function are preserved. The diagnosis of brain death is based on persistent absence of all cerebral and brainstem function, including a lack of response to external stimuli, and no brainstem reflexes (eg, pupillary response, and oculocephalic, corneal, and vestibular reflexes). Reevaluation of the patient in six hours is recommended, and a 24-hour observation period is needed in cases of postanoxic damage (Wijdicks, 1995). It is mandatory to rule out other causes of brain suppression in these cases. Therefore, glycemia, toxic agents, and anesthetics must be checked, and hypothermia reversed (Commichau, 2006).

The diagnosis can be supported by EEG study, which shows a complete absence of electric activity (isoelectricity), and other complimentary tests (transcranial Doppler ultrasound or radionuclide brain diffusion studies), which confirm an absence of cerebral blood flow (Commichau, 2006).

The legal criteria may vary between countries, but usually, two different doctors are required to demonstrate complete absence of brain activity, and this fact can be supported by two flat EEGs taken 24 hours apart (Wijdicks, 1995).

4.5 Posthypoxic neurologic sequelae

After a hypoxic event, patients can develop various sequelae, including a persistent vegetative state, as mentioned above, cognitive impairment with or without extrapyramidal signs, Korsakoff syndrome, parkinsonian syndrome with cognitive impairment (mostly related to CO poisoning), choreoathetosis, cerebellar ataxia, intention (action) myoclonus, and seizures. When ischemia is prominent, two main syndromes are seen, visual agnosia (Balint syndrome and cortical blindness) and “man in the barrel” syndrome (severe bilateral arm weakness) (Commichau, 2006).

5. Electrodiagnostic and neuroimaging studies

Electroencephalography is useful for diagnosing seizures and nonconvulsive status, monitoring the response to antiepileptic drugs, and assessing the patient's prognosis.

However, EEG findings should be interpreted in keeping with the patients' clinical features, and the physician should rule out the presence of drugs, anesthetics, and previous abnormalities. Several abnormal patterns can be seen during and after cardiopulmonary arrest. The absence of detectable EEG activity indicates a poor prognosis. Several authors have attempted to grade EEG activity in postanoxic coma to predict the prognosis. In general, normal or near-normal early activity is assigned a low grade, which represents a favorable prognosis, and conversely, delta activity or a burst-suppression pattern (Fig. 3) are classified as high grades, denoting a poor prognosis (Yamashita et al., 1995). Serial EEG studies can be used to assess the prognosis according to the changes in the patient's grading.

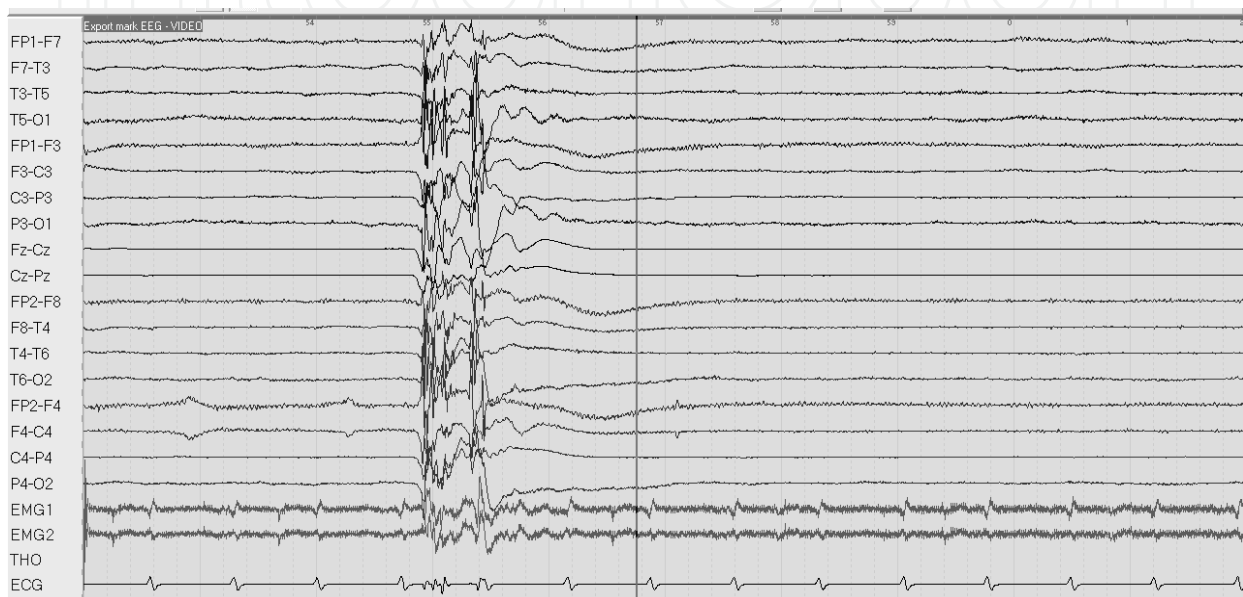


Fig. 3. EEG showing burst-suppression pattern. Courtesy of Dr. M. Veciana.

Evoked potential (EP) studies are also helpful in this regard. Absence of the early cortical components (N20-P27 complex) of somatosensory evoked potentials (SSEPs) (Fig. 4) in a comatose patient three days after cardiopulmonary arrest indicates an ominous prognosis (Wijdicks et al., 2006). To better predict the prognosis in hypoxic/anoxic encephalopathy, clinical examination, EEG, and SSEP results can be combined (Chen et al., 1996).

Cranial CT might not be useful in the first few hours after cardiopulmonary arrest. In a study of patients with nontraumatic out-of-hospital cardiopulmonary arrest, early CT (within 24 hours) was normal in 88%. In the remaining patients, CT showed varying degrees of cerebral edema, usually without herniation. Only one patient showed acute subarachnoid hemorrhage (Cocchi et al., 2010). The most frequent abnormalities found after 72 hours are bilateral hypodensity of the globi pallidi, diffuse leukoencephalopathy, and hypodensities corresponding to ischemia of watershed zones (visual cortex, visual association areas, superior parietal lobules, primary sensory and motor cortices, cerebellar cortex, basal ganglia, and thoracic spinal cord) (Commichau, 2006). MRI can provide higher resolution for brain imaging, but it may be difficult to perform in a patient under ventilatory support.

Lastly, one biomarker found to be of use is serum neuron-specific enolase concentration above 33 g/L, which is predictive of a poor outcome (Wijdicks et al., 2006), although this cut off is currently under revision (Oddo & Rossetti, 2011).

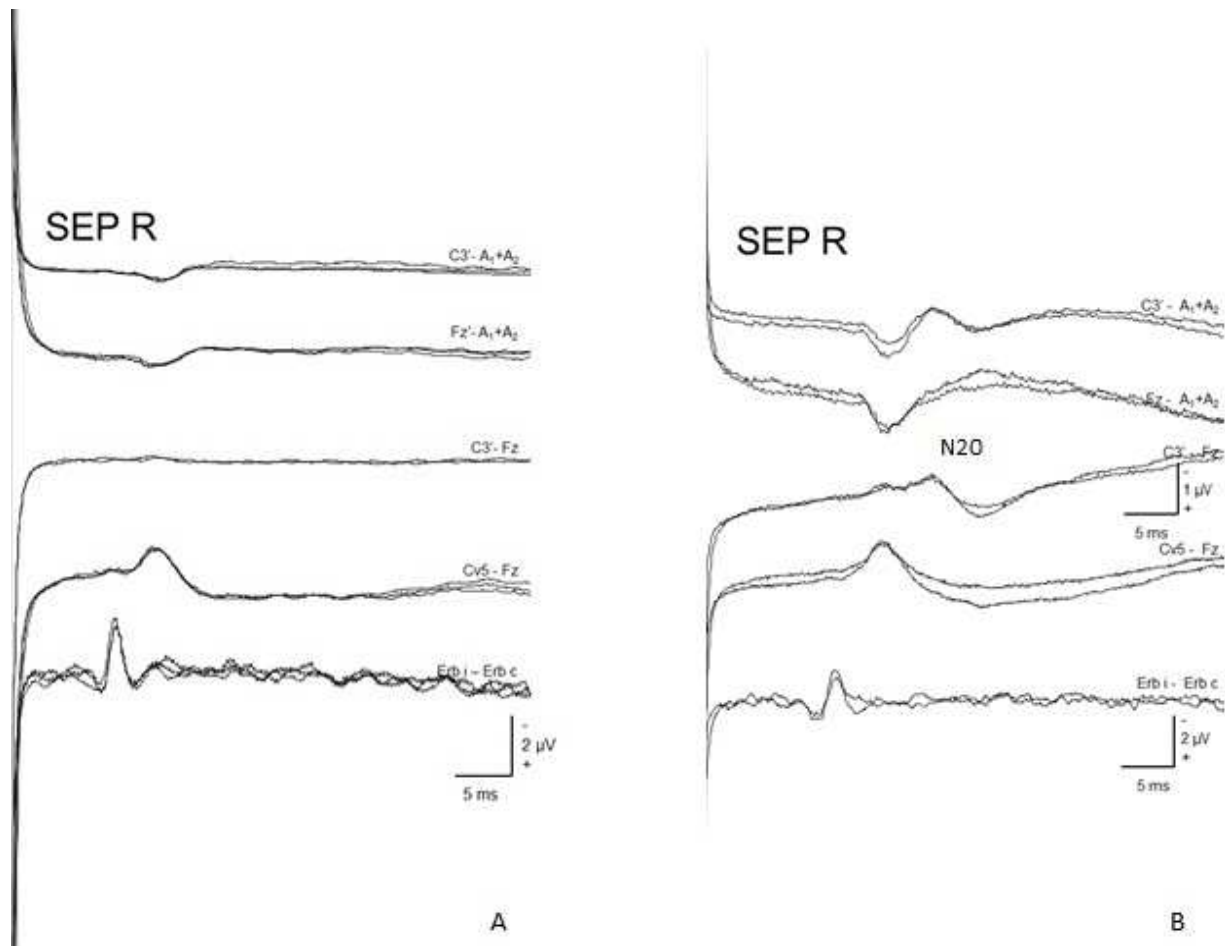


Fig. 4. Somatosensory evoked potential (SSEPs) registers. A: Absence of the early cortical components (N20-P27 complex). B: Normal SSEP. Courtesy of Dr. M. Veciana.

6. Treatment

Treatment for postanoxic encephalopathy can be divided into strategies focussed on treating the acute or chronic associated complications and approaches directed toward protecting the brain during the recovery process and preventing further hypoxic injury.

It is critical to reestablish cardiac and pulmonary function as soon as possible. Once this is accomplished, there is considerable evidence that hypothermia can be of use to avoid further brain damage (Arrich, 2010; Hypothermia after Cardiac Arrest Study Group, 2002; Bernard et al., 2002). Therefore, following hypoxic/anoxic injury to the brain, patients should undergo conventional cooling to achieve mild therapeutic hypothermia (Arrich, 2010). Other treatments such as administration of barbiturates (Brain Resuscitation Clinical Trial I Study Group, 1986), vasodilator drugs (Geocadin et al., 2008), calcium channel blockers (Brain Resuscitation Clinical Trial II Study Group, 1991), and steroids (Jastremski et al., 1989), although theoretically of use, have not shown substantial benefit. Oxygen could be beneficial within the first hours, but does not seem helpful once the blood becomes oxygenated (Brain Resuscitation Clinical Trial I Study Group, 1986).

Efforts should be directed to maintain the balance of other factors such as cerebral perfusion, and avoid additional potential injury related to cerebral edema, intracranial hypertension, fever, and hyperglycemia. To maintain cerebral perfusion, a median arterial blood pressure of 80 to 100 mm Hg is suggested to be beneficial within the first 24 hours after cardiac arrest (Bell et al., 2005). Monitoring by neurological examination is useful to promptly detect any worsening due to intracranial hypertension and brain herniation. Hypoxia, hypotension, and hypercapnia can worsen brain damage and should be avoided. Hyperventilation can also be harmful. Therefore, it has been suggested that comatose patients should be mechanically ventilated to achieve normocapnia (ECC, 2005). Hypoglycemia and hyperglycemia can both produce brain damage after any brain injury; hence, strict control of glycemia is needed during this period (Losert et al., 2008).

Management of seizures requires special attention, as there is evidence that strict seizure control can improve the prognosis of patients who have experienced cardiopulmonary arrest (Rossetti et al., 2009). Seizures and myoclonus are common following anoxic brain injury (Koenig & Geocadin, 2005), although prophylactic treatment for these events is not an extended practice. Whenever seizures are suspected, EEG study should be performed, and if positive, antiepileptic drugs should be promptly administered. Axial myoclonus responds poorly to anticonvulsant therapy. Benzodiazepines and sodium valproate may be effective, although more aggressive treatment, such as neuromuscular blockade or deep sedation with midazolam or propofol, is sometimes required (Koenig & Geocadin, 2005).

On a longer-term basis, complications such as mood disorders (depression, disinhibition, agitation, apathy, and mania) will require proper medical therapy. Cognitive impairment can be managed with cognitive stimulation, and motor disorders with rehabilitation therapy.

7. Delayed postanoxic encephalopathy

Lastly, and regarding our case report stated below, we will take a moment to discuss delayed postanoxic encephalopathy. DPE is a rare condition that presents after apparent recovery from acute cerebral anoxia (Custodio & Basford, 2004; Plum & Posner, 1992; Choi, 1986). It appears within one to three weeks after anoxia and has an insidious onset characterized by cognitive, neuropsychiatric, motor, and extrapyramidal abnormalities (Custodio & Basford, 2004; Plum & Posner, 1992). At onset, the patient shows apathy, confusion, attentional and memory deficits, irritability, and aggressiveness, followed by altered gait, spasticity, and extrapyramidal manifestations, which, in some cases, eventually lead to coma or death (Plum & Posner, 1992; Choi, 1986). Some patients stabilize and are left with mild or moderate sequelae, whereas others recover completely (Custodio & Basford, 2004).

DPE has been related to acute CO poisoning (Custodio & Basford, 2004), connatal and postoperative anoxia, cardiopulmonary arrest of any cause (heart disease, heroin intoxication (Protass, 1976)), hypovolemic shock, hypoglycemia, and strangulation (Custodio & Basford, 2004; Ginsberg, 1979; Hori et al., 1991).

The main histopathological patterns seen in this syndrome are demyelination in the centrum semiovale and necrosis of the cortical laminae and basal ganglia, which correlate with cranial MRI features (Custodio & Basford, 2004; Hori et al., 1991). On neuroimaging, DPE patients show increased signal intensity on T2-weighted and FLAIR sequences, repercussions in diffusion-weighted images and ADC mapping of the centrum semiovale and periventricular white matter, and bilateral signal abnormalities in the globi pallidi, with low signal intensity on T1-weighted and high signal intensity on T2-weighted and FLAIR images (JH Kim et al., 2003; Inagaki et al., 1997). It is reasonable to assume that the abnormal features in the pallidal nuclei are secondary to acute damage after anoxic injury, whereas the white matter findings correspond to delayed damage.

Outcome in DPE ranges from complete recovery to death, and seems not to be related to the medication administered (Custodio & Basford, 2004; Kwon et al., 2004). Severity and persistence of DPE sequelae have been correlated to the presence and persistence of low signal intensity in the ADC map on cranial MRI (JH Kim et al., 2003). The outcome in our patient was favorable and coincided with an improvement in the white matter lesions on FLAIR imaging, despite the presence and persistence of low signal intensity in the ADC map.

8. Case report

A 34-year-old man with a history of weekly inhaled cocaine use was brought unconscious to the emergency room. He gradually regained consciousness and became responsive and alert. Neurological examination and cranial computed tomography (CT) findings were normal. Urine tests were positive for heroin and cocaine. Based on this fact and the absence of other causes of respiratory depression, a diagnosis of acute respiratory depression secondary to acute cocaine and heroin intoxication was established.

Two weeks later, the patient presented progressive deterioration of cognitive tasks and was unable to carry out daily life activities. His performance at work was impaired and he showed memory loss, attentional deficit, indifference, irritability, and dysarthria. The neurological examination revealed bilateral asterixis, anterograde memory disorder, inattention, and anosognosia; the Mini-Mental score was 17/30. Cranial CT showed bilateral hypodense areas in the globi pallid (Fig. 5).

Cranial magnetic resonance imaging (MRI) revealed high signal intensity on T2-weighted, FLAIR and isotropic diffusion-weighted images, with low ADC values (Fig. 6), consistent with diffuse supratentorial leukoencephalopathy. Neuropsychological examination disclosed a frontal dysexecutive syndrome with moderate memory deficits.

One month later, the patient and his family reported a slight subjective improvement as indicated by a greater ability to concentrate and retain new information. This was in accordance with a reduction in white matter damage on cranial MRI (Fig. 7) and an improvement in the neuropsychological examination.

One year later, the patient showed further improvement and was almost asymptomatic, with only some persistent irritability and attentional deficit. He refused additional cranial MRI and neuropsychological testing, considering himself cured.



Fig. 5. Cranial CT showing bilateral hypodense areas in the globi pallid

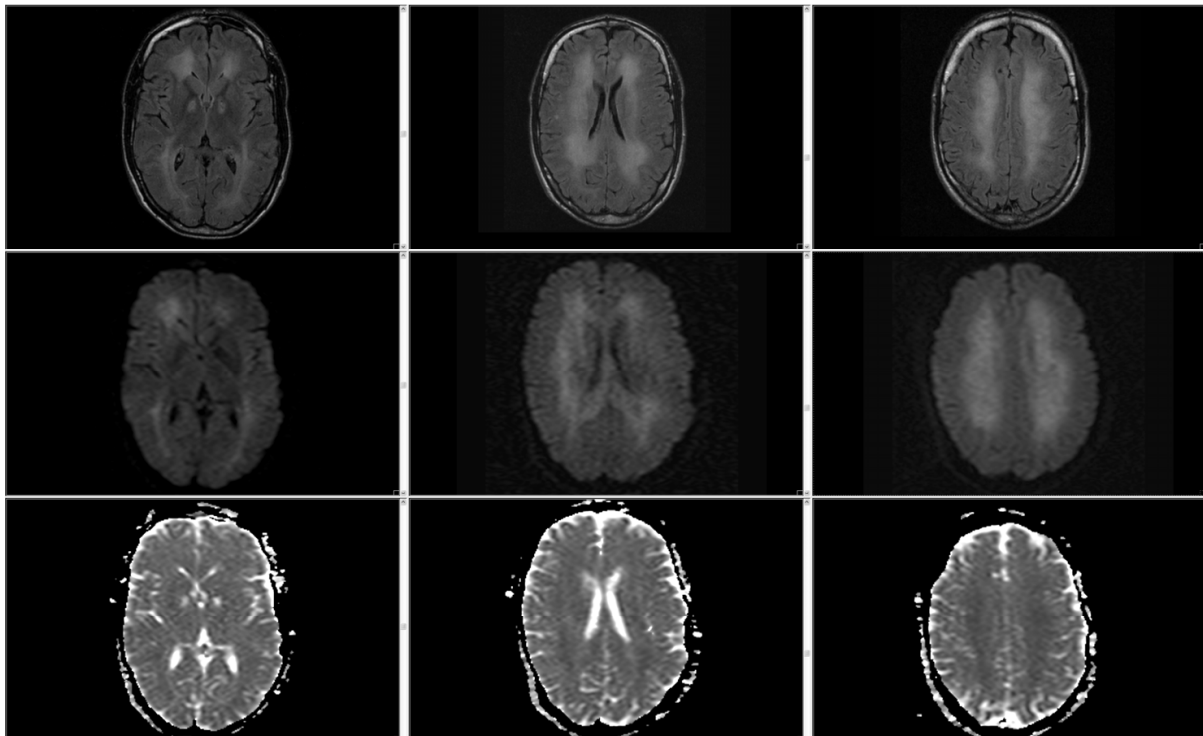


Fig. 6. Initial magnetic resonance imaging findings. FLAIR images (a) show high signal intensity areas in the bilateral periventricular white matter and pallidal nuclei. DWI imaging (b) show similar high signal intensity in the periventricular white matter, with diffuse low signal intensity in the ADC map (c).

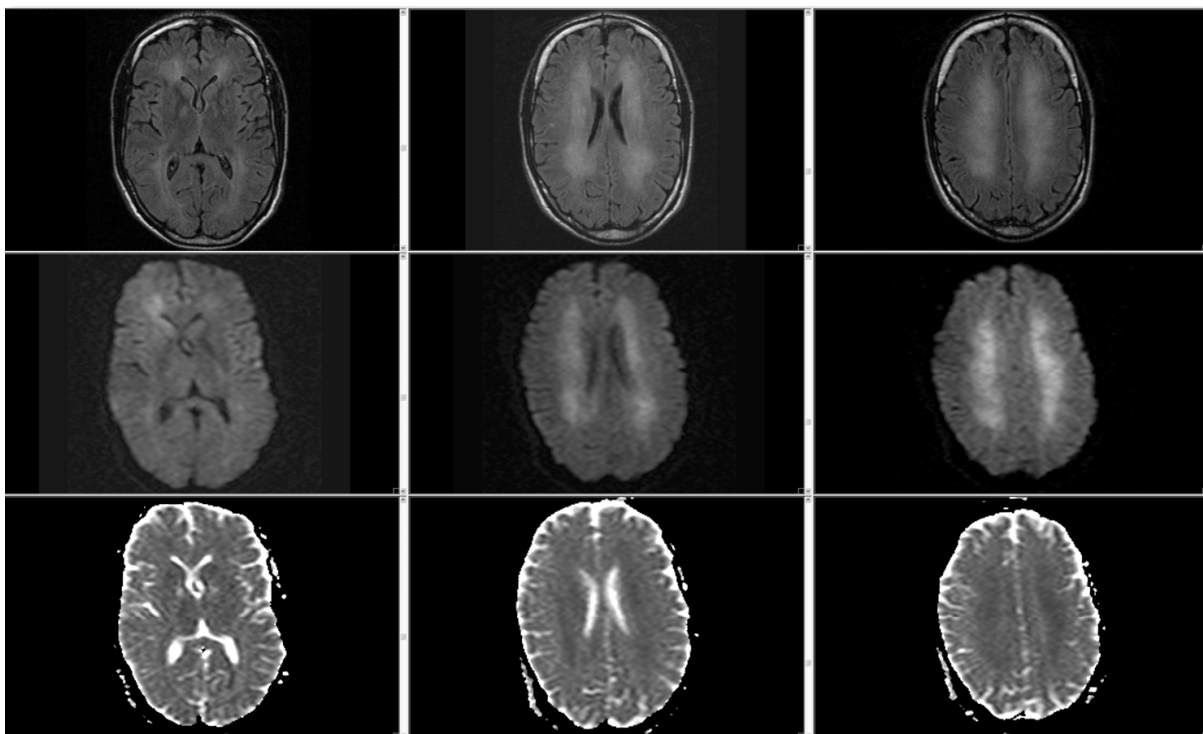


Fig. 7. Follow-up magnetic resonance, one month later, shows a reduction of white matter damage in the bilateral frontal corona radiata and pallidal nuclei (a), and persistence of DWI findings (b) with diffuse low signal intensity in the ADC map (c).

9. Summary

Although huge advances have been made in intensive care medicine and cardiovascular therapy, brain injury remains the main cause of disability in patients who experience cardiopulmonary arrest. Complications are common and their treatment, of crucial importance, although a great amount of medical resources are required. The results of research in various neuroprotective strategies have been discouraging, with the exception of hypothermia, which seems to be a successful and worthwhile measure, as well as therapies focused on seizures. Efforts must be placed on creating new hospital protocols that emphasize the importance of achieving mild hypothermia within the first hours after cardiopulmonary arrest, as well as detecting and promptly treating any kind of seizure.

Regarding delayed postanoxic encephalopathy, we should suspect this syndrome in patients who have suffered respiratory depression or cardiac failure of any cause, or when a patient presents with a subacute onset of cognitive and neuropsychiatric deficits. The clinical evolution of this condition may be favorable, does not seem to depend on any medical treatment, and could be related to an improvement in white matter lesions.

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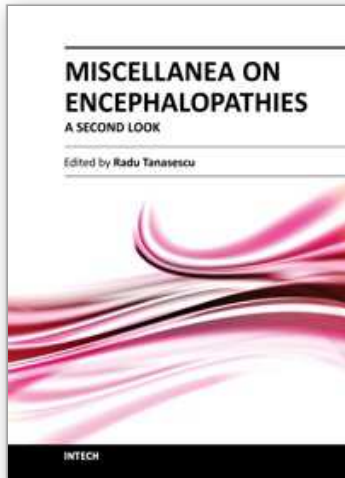
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