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Diagnosis of brain death

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ABSTRACT:
The diagnosis of brain death is based on a series of clinical elements, while forensic confirmation relies on paraclinical investigations to reinforce the clinical diagnosis. The transition to a state of cephalic death occurs in a well- defined clinical context, and is most likely to occur in patients suffering from cerebral vascular accident, head trauma or post-anoxic encephalopathy. As a result, the incidence of cephalic death is higher in neuro-resuscitation. The intensive care physician must be able to make this diagnosis, and then ensure the resuscitation of the brain-dead donor to guarantee the quality of the grafts, since it is from this donor that multi-organ harvesting can be carried out. The brain- dead donor is an unavoidable solution for obtaining transplants, given the limited number of transplants available and the consequent long waiting lists for organ failure patients.

Keywords: Brain death, clinical diagnosis, paraclinical confirmation, cerebrospinal cord injury.

INTRODUCTION:

Encephalic death (ED) is defined as the irreversible destruction of all cerebral functions in the brain, as a consequence of cerebral circulatory arrest, in a subject with a beating heart [1]. In ED, organs remain functional, provided appropriate resuscitation is given, Encephalic destruction suppresses central control of respiration, and regulation of circulatory, thermal and endocrine homeostasis [2].

Epidemiology:

Encephalic death (ED) is evoked by a clinical diagnosis and confirmed by paraclinical examinations.

Incidence of brain death:

The incidence of encephalic death (ED) varies from one country to another. In France, most studies report a rate of 1 to 2% of all hospital deaths, whereas in Spain, where ED is more actively recorded, the rate is 2% [3]. Similarly, the incidence of ED varies from one department to another, with a higher rate in intensive care units. In France and other countries, ED is estimated to account for 7 to 13% of deaths, with the number of potential donors ranging from 3,300 to 3,800 per year [1]. The rate is higher in neuro-intensive care units, which specialize in the treatment of cerebral palsy, reaching 15-20% of deaths.

Causes of brain death:

Encephalic death syndrome (EDS) complicates many serious acute neurological pathologies, in particular [4] stroke. traumatic brain injury and post-anoxic encephalopathy.

Diagnosis of cephalic death:

The clinical assessment of neurological status is the key element in the diagnosis of ED, and must be carried out rigorously, after eliminating confounding factors that may modify clinical and paraclinical examinations.

Table 1: Confounding factors [5].

Confounding factors
-Metabolic disorders
-Hyponatremia
-Hypoglycemia
-Hypercalcemia
-Severe liver failure
-Acid-base disorders
-Endocrine disorders
-Adrenal insufficiency
-Thyroid insufficiency
-Hypothermia (<35 ◦C)
-Shock (mean arterial pressure <50 mm Hg)
-Drug treatments
-Barbiturates, benzodiazepines, morphine, propofol
-Poisoning, intoxication
-Trichloroethylene, methoqualone, meprobamate, baclofen

-Curarization
-Severe cervicofacial trauma
- Ocular damage , complex facial fractures

Clinical diagnosis:
The clinical diagnosis of encephalic death in ED is based on three clinical criteria which must be simultaneously present.
Deep coma with a Glasgow score of 3, flaccid and reactive. The absence of reactivity is sought by applying painful compressions at the following sites [6] the nail bed, the supraorbital nerve at its emergence and the temporomandibular joint, Pierre-Marie et Foix maneuver.
Deep reflexless coma corresponds to the absence of spontaneous and CNS- controlled movements. Spinal reflexes and movements may persist [3] [7], in 10-30% of cases, such as arm flexion, limb elevation, deep inspiration and opisthotonos, which are described as "LAZARE syndrome".

Abolition of brainstem reflexes, i.e. :
- **Photomotor**: pupils are in an intermediate position and insensitive to light stimuli
- **Corneal**: touching the cornea with a sterile compress is not accompanied by eyelid movement.
- **Oculovestibular**: head rotation is not accompanied by eye movement.
- **Oculo-cardiac**: compression of the eyeballs does not cause reflex bradycardia.

Absence of spontaneous ventilation:
confirmed by a hypercapnia test. This consists of [8] :
- Pure oxygen ventilation with FIO2 at 1 for 15 minutes in normocapnia.
- Disconnection for 10-15 minutes.
- Endotracheal oxygen via small-bore proximal probe (5-8 l/min) or T-piece.
- SpO2 monitoring is essential.
- The duration of this test is usually 10 to 15 minutes.
- In apnea, a PaCO2 close to 60 mm Hg is required to confirm the absence of respiratory movements.

Paraclinical examinations:
For the purposes of donation, the clinical diagnosis of ED must be confirmed by one of the complementary examinations required by law.
The disappearance of recordable cerebral electrical activity and the absence of cerebral perfusion are the 2 medico-legal criteria for the paraclinical diagnosis of ED [5]. The criteria for choosing one or other of these examinations are as follows [9] :
- 100% specificity and high sensitivity.
- Be rapidly available and accessible, possibly at the patient's bed in the case of an unstable patient.
- Be non-toxic, to avoid any limitation of sampling due to the procedure's methodology.
- Be easily interpretable.
- Be legally valid in the country where it is performed.

Paraclinical examinations of forensic value:
Electroencephalogram (EEG) This test has forensic value in the diagnosis of ED, provided that two EEGs are performed 4 hours apart, which are considered null and reactive. During a 30-minute recording period, the maximum amplitude is greater than 5 µV [10]. The major advantage of EEG is that it is non-invasive, easily reproducible and available day and night. The limitations of this examination are :
- It does not explore the entire brain (thalamus and brain stem).
- There must be a 4-hour delay between the 2 examinations, which is sometimes problematic in thermodynamically unstable patients.

Cerebral angioscanner:
Angiography is used to confirm encephalic circulatory arrest by demonstrating the absence of opacification of the encephalic branches of the internal carotid and vertebral arteries, objectified by a series of images, the last of which must be taken at least 60 seconds after injection [6], combined with good opacification of the branches of the external carotid artery. It is advisable to wait at least 6 hours between the clinical diagnosis of ED and the angioscanner scan. The advantage of this technique is that it is rapid and minimally invasive. Its limitations are the persistence of arterial images that are difficult to interpret.
Angioscan must be performed on a thermodynamically stable patient, i.e. with MAP > 65 mm Hg and diuresis of at least 100 ml/h [6].

Conventional and digital cerebral angiography:
This is the reference test for diagnosing ED, with 100% specificity even in cases of intoxication or metabolic disorders [6]. It is carried out by venous or arterial route, and aims for the absence of opacification of the internal carotid arteries beyond the supraclinoid segment and of the arteries at the base of the skull 60 seconds after injection. The absence of internal cerebral venous drainage provides further evidence of the cessation of cerebral vascularization [6]. Its limitations are its invasive nature, with the risk of renal toxicity associated with injection of the iodinated contrast medium.

Paraclinical examinations with no forensic value:
Magnetic resonance angiography (MRA)

This examination is similar to angioscanner, but takes longer to perform, and poses a problem of availability. It also requires resuscitation equipment adapted to the magnetic environment.

Technetium-99mTc-HMPAO isotope angiography:
The only examination capable of testing both cerebral perfusion and neuronal metabolism. This minimally invasive examination has medico-legal value in some countries, and meets the definition of ED. However, its indication is limited by the problem of accessibility: ED is demonstrated by the juxtaposition of "empty skull" images due to the absence of encephalic perfusion, and by the preservation of perfusion in the external carotid territory.

Paraclinical examinations with predictive value for initiation of the ME process:
Evoked potentials:
They correspond to the recording of the electrical signal produced by the nervous system from the periphery to the nerve centers in response to a specific sensory stimulus: somatosensory evoked potentials (SEP), auditory evoked potentials (AEP), visual evoked potentials (VEP) and are based on both the disappearance of all peaks corresponding to intracranial nerve generators and the persistence of activities of extra-cranial origin. The collection of multimodal evoked potentials (EPs) could improve the speed and reliability of diagnostic confirmation [6], particularly in patients impregnated with sedative drugs [2]. EP is less sensitive than EEG to environmental interference, and can determine the disappearance of cortical and subcortical activity, even in the presence of drug intoxication or hypothermia.

The bispectral index (BIS) :
Initially used in anesthesiology and intensive care to assess the depth of sedation. Thanks to continuous monitoring of brain activity, the BIS index can be used to detect the moment of transition to ED (BIS index = 0) [11]. It cannot be used to diagnose encephalic death, but it can be used to determine the appropriate time for confirmatory paraclinical examinations [12]. The BIS suffers from the same limitations as the EEG.

Transcranial Doppler (TCD):
This examination has a specificity of 99% and a sensitivity of 95% [9], and enables cerebral blood flow to be assessed both at the level of the middle cerebral artery, which receives 80% of cerebral flow, using the transtemporal window, and at the level of the basilar trunk, using the suboccipital window. Circulatory arrest is evidenced by retrograde diastolic flow, followed by the appearance of brief, low-amplitude protosystolic peaks, before the signal disappears completely at the stage of vessel collapse [13]. Transcranial Doppler can only be used in an attempt to reduce the delay between the diagnosis of clinical suspicion and the transition to ED state [14]. It can be used to determine the ideal time to move the deceased in order to carry out a paraclinical examination of forensic value. However, it is advisable to wait at least 4 hours before performing an angioscan [15]. The main limitation of transcranial Doppler is insonation difficulties in 20% of patients [5].

Two aspects are characteristic of cerebral circulatory arrest [14] [20]:
Reverse flow, anterograde in systole, retrograde in diastole -Low-amplitude protosystolic peaks. For the diagnosis of ED state, the absence of flow on DTC is not a criterion for cerebral circulatory arrest, as this may be due to the absence of a bone window.

Regulatory aspects of the diagnosis of encephalic death:
The legislation governing the diagnosis of ED differs from one country to another. In the United Kingdom and Switzerland, the diagnosis is confirmed solely by the presence of clinical signs. In Algeria, it is confirmed by the
presence of clinical signs and paraclinical confirmation through two EEGs or angiography, while in Belgium the legislation requires doctors to follow the most recent state of science to confirm the diagnosis [16].

CONCLUSION:
The diagnosis of cephalic death is a key factor in triggering organ and tissue procurement procedures from the deceased donor. It is evoked in a particular etiological context, established by clinical criteria and confirmed by paraclinical investigations.

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