Neuroendocrinological Aspects in Cases of Brain Death After Severe Brain Injury

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Introduction

In evaluating the clinical state of patients with a severe brain injury, the actual brain function can be determined by an examination of the central and the peripheral reflexes (5, 11). Additional information is obtained from the course of the laboratory and clinical findings, the electroencephalogram (EEG) and the cerebral angiogram. In practice, not all of these investigations will always be available or necessary (7). In case of the brain death e.g. of a kidney-donor however, the absent blood supply to the brain must be demonstrated by cerebral angiography. If the contrast-medium stops before reaching the base of the skull, one can conclude that there is also a failure of the blood supply to the Hypothalamic-Pituitary-System, and as a result of this, the whole neuroendocrine system is not perfused. The purpose of the present investigation was to find out whether patients after a severe brain injury with signs of brain death can be stimulated neuroendocrinologically, and if so, whether there are certain patterns of behaviour.

Material

Twenty patients were investigated, 6 female and 14 male aged between 15 and 63 years (average age 31.3 years). Seven patients were surgically treated, whilst in the other 13 patients surgical treatment was either not necessary or not possible. Because of technical reasons, or rather because of cessation of the circulation of the blood, brain death could not be documented by angiography or EEG in all of the patients. None of the patients however showed any central reflexes when they were examined. In two patients, angiography showed contrast medium in the area of the "PICA" (posterior inferior cerebellar artery), three showed a retarded internal carotid artery picture. The stimulation test was performed with 200 µg TRH (thyrotrophin-releasing hormone), 100 µg LH-RH (luteinizing hormone releasing hormone) and 500 ml of a 6 per-cent Arginin-Hydrochloride solution infused over a period of 30 minutes. After the determination of the basal level, blood was taken at intervals of 15, 30, 60, 90 and 120 minutes. The determination of the hormones was accomplished by Radioimmunoassay (RIA). The human growth hormone (HGH), prolactin (hPRL), luteinizing hormone (LH) and thyrotropin (TSH) were ascertained. In evaluating the TSH, a co-existent hyperthyroid metabolic state was excluded by a simultaneous analysis of triiodothyronine (T₃) and thyroxine (T₄). In addition, the spontaneous fluctuations of cortisol were measured.
Results

From the neuroendocrinological point of view the patients with brain death behave differently. Even the individual specific functions may differ within the same patient. There are, however, nearly always elevated basal levels in patients who have only a short survival time; whilst patients who are treated over a longer period show lower basal levels. This fact is also demonstrated by the fall in the average values when examinations are repeated within the same patient. In contrast to the HGH where one can see a weak or delayed response in only two of 20 patients, the levels of hPRL, TSH and LH occasionally show a distinct response. Patients with high hPRL levels resulting from the absence of prolactin-inhibiting-factor (PIF) can be partly stimulated by the TRH in the anterior pituitary lobe. The intact function of adenohypophysis for hPRL is recorded also in this particular case by a simultaneous increase in TSH. In case of a low hPRL, two groups of patients can be identified. One group shows a general pituitary insufficiency whilst the other one shows only a partial pituitary insufficiency. This phenomenon can be explained by a dependence on the dosage of the administered TRH. After the administration of LH-RH there is a definite tendency for the level of LH to rise. For example an eighteen years old female patient showed a distinct increase of LH in response to LH-RH, at a time when brain death had already been confirmed for over 24 hours. Even in one patient who had been treated for over 8 days a release of LH can be achieved. This effect is specific for LH, since all the other hormones mentioned above showed no response. A definite response from TSH was achieved only twice, 80 percent of the patients examined showed spontaneous fluctuations at or below basal levels. Apart from the above-mentioned dependence on the dosage of the releasing hormone for TSH response, pharmacological effects of current medication (e.g. phenytoin, steroids) have to be taken into consideration. Finally the measured cortisol levels show only random fluctuations around a variety of individual values. This leads to the assumption that the corticotrophin (ACTH)-cortisol-axis has been disrupted. If there are excessively high measured cortisol levels, these will not be observed to fall following therapeutic dexamethasone.

Discussion

It has to be noted that with so-called brain death, documented by angiography and EEG, a loss of function of the Hypothalamic-Pituitary-system need not be present in every case (6). Even if one excludes a documented intracerebral blood supply, the releasing hormones which have been given intravenously seem to be able to reach the hypothalamic-system by vascular or non-vascular means. The traumatic events at the adenohypophysis and at the hypothalamus itself which can cause a dissociated partial function, are especially important (2-4, 8, 10). The weak or delayed response of the levels of hormones and the random fluctuation cannot always be rigidly separated. Furthermore it has to be said that it cannot be the topic of this investigation to modify or discuss the clinically defined concept of brain death but to find out whether homogenous neuroendocrinological patterns of behaviour can be recognized whenever brain death occurs. This does not seem to be the case.