Rapidly progressive dementia as a form of presentation of Cushing syndrome☆

Demencia rápidamente progresiva como forma de presentación del síndrome de Cushing

Cushing syndrome is a rare entity with an estimated prevalence of one case per 26 000 population, although the subclinical form seems to be more frequent. The disease predominantly affects women; incidence peaks between the ages of 25 and 40 years. The manifestations of this systemic disease include psychiatric alterations, particularly depression, in up to 66% of cases.[1] The syndrome rarely causes dementia, however. Screening for Cushing syndrome is recommended in patients with rapidly-progressing Alzheimer-type dementia,[2] especially when accompanied by hypokalaemia[3]; several cases have been reported of dementia triggered by endogenous hypercortisolism, a potentially reversible cause.

We present the case of a 68-year-old woman with a history of arterial hypertension, diabetes mellitus, dyslipidaemia, resected adenocarcinoma of the colon, and 2 hospital admissions due to perforated diverticulitis. She visited our department due to a 2-year history of progressive gait impairment without a diagnosis, in addition to a 5-month history of behavioural alterations in the form of disinhibition, deterioration of language skills, and self-neglect. The examination revealed frontal lobe syndrome characterised by inattention, perseverance, bradyphrenia, near-total lack of language with delusional content, frontal release signs, inability to perform rapid alternating movements, and proximal limb weakness compatible with myopathy. A diagnostic study revealed generalised cortical atrophy on CT images and multiple biochemical alterations: hypernatraemia (156 mEq/L), hypokalaemia (2.98 mEq/L), metabolic alkalosis (pH 7.61, pCO_2 41 mm Hg, HCO_3 41 mM), poor glycaemic control in the preceding months (9% glycated haemoglobin), neutrophilia (6600 neutrophils/μL), lymphopaenia (600 lymphocytes/μL), eosinopaenia (no eosinophils), elevated ESR (65 mm), and hypoproteinaemia (5.1 g/dL). A urine test revealed hyperglycosuria (1005 mg/dL) and slightly elevated potassium levels (83.4 mEq/L). These findings led us to suspect a hormonal disorder. An extensive hormone study revealed high serum and urine cortisol levels (44.91 μg/dL and >1500 μg/L, respectively), ACTH oversecretion (88.36 pg/dL), subclinical central hypothyroidism (TSH 0.37 μIU/mL, free T3 1.21 pg/mL, free T4 0.81 ng/dL), and hypogonadotropic hypogonadism (FSH 0.21 mIU/L, LH <0.100 mIU/L). A brain MRI scan revealed a pituitary macroadenoma eroding the sella turcica. We suspected Cushing syndrome secondary to an ACTH-producing macroadenoma; low-dose and high-dose dexamethasone suppression tests yielded negative results. These findings, combined with the remarkably high urine cortisol levels (a rather infrequent finding in cases of central hypothyroidism) and the normal results of a body CT scan, ruled out the presence of a synchronous ACTH-secreting tumour. After diagnosis, metabolic imbalances were corrected and the patient started treatment with spironolactone, metyrapone, and ketoconazole until endogenous cortisol production was suppressed, after which she received hydrocortisone. Higher cortical functions improved considerably within 2 weeks, especially in terms of behaviour, and the patient recovered language fluency and coherence. During that period, she underwent 3 electroencephalography (EEG) studies. The first was conducted after an episode of behavioural alterations before she was admitted to hospital; no abnormalities were found. The second study, performed upon admission, revealed non-specific slow activity in both frontal regions. The third study, performed after suppression of endogenous cortisol production, found no alterations. The patient was transferred to the endocrinology department for medical treatment; while awaiting surgery, she presented upper gastrointestinal bleeding and died several days later due to septic shock.

We present a case of rapidly progressive frontotemporal dementia, with neuropsychiatric symptoms resolving after controlling metabolic imbalances associated with Cushing syndrome secondary to an ACTH-producing pituitary macroadenoma. Although dementia is a rare manifestation of the condition, hypercortisolaemia may accelerate the progression of Alzheimer-type dementia,[3] and has been proposed as the only direct cause of this type of dementia,[4] although in cases of cortical involvement, which was not the case with our patient. The condition develops due to the presence of glucocorticoids in the brain; these are mediated by 2 types of receptor: type I receptors have greater affinity and are mainly expressed in the hippocampus and limbic system; type II receptors require higher concentrations of the ligand to be activated and are distributed in several different brain regions. Experimental studies have shown neuronal changes secondary to elevated glucocorticoid levels; these include reversible dendrite atrophy in hippocampal CA3 pyramidal neurons[5] and alterations in intracellular calcium concentration. At a macroscopic level, patients display reduced hippocampal volume and generalised cerebral atrophy.[6] These findings are correlated with functional alterations, mainly amnestic deficits. A significant decrease in cortico-cortical connections has been observed in patients with hypercortisolism, which is in turn associated with cortical atrophy.[7] Young patients with Cushing syndrome and no neuropsychiatric symptoms have been found to have indirect signs of cerebral atrophy, including increased ventricular size; these changes are partially reversible by correcting hypercortisolaemia with pituitary or adrenal surgery.[8] In symptomatic patients, surgery has been found to resolve psychiatric manifestations and halt the progression of cognitive impairment[3]; this underscores the importance of correctly identifying this entity in patients with dementia.

Follow-up EEG studies constitute another interesting aspect of the case presented here. In a series of 33 patients with Cushing syndrome, EEG revealed either normal patterns or non-specific alterations in the form of slow,

☆ Please cite this article as: Rodríguez-López C, Guerrero Molina MP, Martínez Salio A. Demencia rápidamente progresiva como forma de presentación del síndrome de Cushing. Neurología. 2019;34:339—340.

disorganised background activity.[9] Our case demonstrates that this variability in EEG readings can be observed within a single patient: our patient displayed both patterns in EEG recordings taken several days apart while experiencing acute neuropsychiatric symptoms. This shows that this test is not useful either for diagnosis or for clinical follow-up.

To our knowledge, this is the first published case of frontotemporal dementia in the context of Cushing syndrome. The patient died from unrelated causes, which prevented postsurgical follow-up and the long-term collection of clinical and radiological follow-up data. We were therefore unable to determine whether the patient had underlying subclinical frontotemporal dementia aggravated by Cushing syndrome, or whether alterations were due to hypercortisolism.

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2173-5808/

Duret haemorrhage during intravenous administration of thrombolytic therapy☆

Hemorragia de Duret durante la perfusión de tratamiento fibrinolítico

Dear Editor:

Symptomatic intraparenchymal haemorrhages are an infrequent complication of fibrinolytic treatment (appearing in 1.7%-4.6% of cases), with a mortality rate of 54%-75%.[1—3] Up to 55% of these haemorrhages (3.3% of all patients treated) involve a remote location with regards to the area of infarction.[3,4]

We present the case of a patient who died after a massive brainstem haemorrhage, possibly secondary to a transtentorial herniation (Duret haemorrhage) during treatment of a proximal occlusion of the right middle cerebral artery (MCA) with intravenous recombinant tissue plasminogen activator (rt-PA). Our patient was a 59-year-old Romanian woman with obesity and arterial hypertension of unknown progression time, treated with angiotensin-converting enzyme (ACE) inhibitors; the patient presented sudden-onset left hemiparesis and dysarthria. On the way to hospital, unknown atrial fibrillation was detected, with controlled ventricular response and arterial pressure of 200/100 mm Hg, subsequently decreasing without administration of antihypertensive treatment. Upon arrival, we observed right hemispheric syndrome (NIHSS = 13). The emergency blood analysis showed macrocytosis without anaemia (Hb 13.9 g/dL, MCV 106.5 fL), platelets and leucocytes within normal ranges, and INR values at the higher threshold of normality (1.28) with normal thromboplastin time. A multiparametric brain CT scan (baseline brain CT scan, CT perfusion, and CT-angiography) revealed occlusion of the right distal M1 segment, with no established infarct on the baseline brain CT scan, and symmetrical cerebral blood volume maps with longer time-to-peak in all cortical territories of the right MCA (Fig. 1). After confirming with

☆ Please cite this article as: Quintas S, Palmí Cortés I, Zapata-Wainberg G, López Ruiz R, Vivancos J. Hemorragia de Duret durante la perfusión de tratamiento fibrinolítico. Neurología. 2019;34:340—342.