Cushing’s Syndrome, Cortisol, and Cognitive Competency: A Case Report

Neil Oronskey, Bennett Thilagar, Carolyn M. Ray, Scott Caroen, Michelle M.C. Lybeck, Lindsey Ferry, Ronald A. Voves, Bryan Oronskey

Keywords
Cushing’s syndrome · Carcinoid patient · Glucocorticoids · ACTH · Immunosuppression · Neurocognitive impairment · Advanced directives

Abstract
Glucocorticoids are associated with immunosuppression and neuropsychiatric complications. We describe the case of a carcinoid patient with Cushing’s syndrome (CS) and neurocognitive impairment due to ectopic ACTH production who developed sepsis and died because of his family’s decision to withdraw antibiotic treatment. This report is presented to illustrate the importance of advanced-care planning in patients with CS.

Introduction
Cushing’s syndrome (CS) is a general term for a cluster of endocrine abnormalities characterized by chronic cortisol overproduction. Characteristic clinical comorbidities include metabolic complications (e.g., visceral obesity, diabetes mellitus, and dyslipidemia), cardiovascular complications (e.g., systemic arterial hypertension, atherosclerosis, and thromboembolism), bone complications (e.g., osteoporosis and osteoarthritis) infective complica-
tions, and neuropsychiatric disorders (e.g., major depression, mania, anxiety, and cognitive impairment) [1]. CS may be exogenous and iatrogenic due to corticosteroid administration or endogenous due to excessive ACTH secretion, most commonly from a pituitary adenoma, referred to, somewhat confusingly, as Cushing’s disease, or less commonly from a nonpituitary tumor (ectopic CS) and primary adrenal neoplasms [2]. Several studies link untreated CS to fatal infectious complications [3]. This report describes the case of a 60-year-old carcinoid patient with cognitive impairment due to hypercortisolism from CS who developed bacteremia; his condition deteriorated, and he died after a decision was made to withdraw care.

**Case Presentation**

A 60-year-old male with metastatic bronchopulmonary neuroendocrine tumor treated on a clinical trial for over 5 months was admitted to the hospital with complaints of fever, agitation, and weakness. His medical history was significant for newly diagnosed CS secondary to ACTH secretion; he had been hospitalized 2 weeks earlier for CS-induced hyperglycemic crisis. On admission, the patient presented with classic cushingoid habitus of facial plethora, moon facies, muscle atrophy, abdominal striae, and truncal obesity. His physical examination was significant for bilateral crackles and agitation consistent with corticosteroid psychosis. The arterial blood gas analysis on room air was pH 7.497, PaCO$_2$ 29 mm Hg, PaO$_2$ 71 mm Hg, and oxygen saturation 95%.

Laboratory data were significant for hyperglycemia, hypokalemia, and leukocytosis with bandemia. The chest CT scan showed no definite evidence of pulmonary thromboembolism. As respiratory failure was imminent, he was transferred to the intensive care unit and mechanically ventilated. The highest positive end-expiratory pressure and FiO$_2$ required to maintain oxygenation were 5 cm H$_2$O and 50%, respectively. Cultures were taken from bronchial secretions directly after endotracheal intubation and from urine and blood. The patient was diagnosed with *Staphylococcus aureus* bacteremia, and based on susceptibility testing, he was started on vancomycin and Zosyn. In addition to antibiotics, the patient received lisinopril for CS-induced hypertension and insulin sliding scale to control hyperglycemia.

Since high circulating levels of glucocorticoids due to ectopic ACTH secretion predispose to infection and impair immune function and clearance of bacteria, the immediate plan was to start him on mifepristone (600 mg daily) as a glucocorticoid receptor antagonist to counteract the immunosuppressive and cognitive effects of the endogenous hypercortisolism. As soon as the patient’s condition improved (which would have been expected given the known reversibility of hypercortisolism), cytoreductive chemotherapy would have been restarted to reduce the paraneoplastic stimulus. However, the patient’s family with medical power of attorney refused consent and withdrew him from the ventilator. The patient died shortly thereafter.

**Discussion**

Advance directives are written to guarantee autonomy in the event that individual decision-making capacity is lost due to disease severity or treatment [4]. However, as a blanket statement that may contain overly broad (or overly specific) prewritten blocks of text, espe-
cially for cancer patients, the content of advance directives may or may not necessarily apply to and/or the patient’s wishes may or may not be correctly interpreted during acute, temporary and potentially reversible conditions that occur during cancer treatment such as infection due to ectopic CS.

Given the potential for cognitive impairment and other acute sequelae such as difficult-to-treat infections from the development of ectopic CS, this case illustrates the importance of revisiting the advance directive when a medical diagnosis associated with temporary cognitive impairment such as CS is made.

**Statement of Ethics**

The authors have no ethical conflicts to disclose.

**Disclosure Statement**

The authors have no conflicts of interest to declare.

**References**

1. Pivonello, R, Simeoli C, De Martino MC, Cozzolino A, De Leo M, Iacuaniello D, Pivonello C, et al: Neuropsychiatric disorders in Cushing’s syndrome. Front Neurosci 2015;9:129.
2. Tsigos C, Chrousos GP: Differential diagnosis and management of Cushing’s syndrome. Annu Rev Med 1996;47:443–461.
3. Bakker RC, Gallas PR, Romijn JA, Wiersinga WM: Cushing’s syndrome complicated by multiple opportunistic infections. J Endocrinol Invest 1998;21:329–333.
4. Halpern NA, Pastores SM, Chou JF, Chawla S, Thaler HT: Advance directives in an oncologic intensive care unit: a contemporary analysis of their frequency, type, and impact. J Palliat Med 2011;14:483–489.