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Case Reports

Acute Psychosis and Panhypopituitarism: A Case Report

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We present a case of acute psychosis in a patient with panhypopituitarism admitted for adrenal crisis secondary to insufficient glucocorticoid replacement. Three months prior, she was admitted for a similar episode of adrenal crisis and underwent intubation; however, at that time her mental status was normal with no reported episodes of delirium or psychosis. After extubation, she was found to have psychotic symptoms which waxed and waned and were vaguely responsive to antipsychotics. She was ultimately stabilized and discharged, only to return three months later after missing multiple doses of her prednisone. During her current presentation, she had a recurrence of her waxing and waning mental status, which was presumed to be an organic result of her prior hypotension and anoxia vs. a primary psychotic break. In retrospect, it was largely dependent upon whether she received her scheduled steroids. Once her adrenal crisis had passed her cognition improved with daily steroid replacement and antipsychotics were unnecessary.

BACKGROUND

There have been few reports of psychosis as a prominent feature of inadequate glucocorticoid replacement in panhypopituitarism. Initial presentations are often attributed to an undiagnosed psychiatric disorder or vascular collapse during the crisis state causing delirium.[1] Patients often end up being treated with antipsychotics over prolonged periods with minimal benefits while the reversible cause of psychosis remains hidden and comes to light with improvement in the patient's condition with adequate steroids replacement.

CASE PRESENTATION

A 63-year-old female with a past medical history of panhypopituitarism and blindness secondary to a resected pituitary tumor ten years earlier presented with complaints of decreased oral intake, vomiting, altered mental status, confusion, and hallucinations for the past two days. History obtained from the family noted that she was admitted to another hospital for vomiting and presumed sepsis three months prior. At that time, she was hypotensive and acutely decompensated in the emergency department. While she was there, she was intubated and admitted to the intensive care unit. After discharge she was still confused, hallucinating, and had paranoid symptoms that were not present before that admission. She was placed on Quetiapine and corticosteroid of unknown dosage. Levothyroxine was restarted at 75 mcg daily which was her home dose. Subsequently, she was sent to a subacute rehabilitation facility where she remained until coming to our facility.

Before her current admission, she was found to not be taking her corticosteroid replacement as prescribed for approximately two weeks. On presentation, she was again hypotensive with a blood pressure of 64/28, tachycardic with a heart rate of 101 beats/min, and Tmax of 100.7 F. Lab tests showed elevated creatinine of 5.4 mg/dl from a baseline of 0.9 mg/dl (normal 0.5-1.1 mg/dl), lactate of 2.7 mmol/L (normal 0.7 – 2.1 mmol/L), glucose 110 mg/dl (normal 70-99 mg/dl), sodium138 mEq/L (normal136-145 mEq/L), T4 1.02 ng/ml (normal 0.8-1.8 ng/ml), and TSH 0.06 (normal 0.27-4.02). She was presumed to be septic and was given 30cc/kg of fluid bolus and was started on broad-spectrum antibiotics. Blood and urine cultures were sent, and chest imaging showed clear lungs bilaterally. No ACTH or cortisol testing was done at this time; however, she did have an electroencephalogram that showed slow waves without seizure spikes and a brain MRI that was normal.

She was started on 100mg of intravenous hydrocortisone every eight hours with a taper to oral prednisone. Following these measures, her hemodynamic status improved. Blood and urine cultures did not show any growth, her fever resolved, and no source of infection was detected, so she was taken off antibiotics. She was not given mineralocortocoid replacement as per endocrinology recommendations. Her clinical presentation was explained as an adrenal crisis secondary to medication noncompliance. Her altered mental status was initially attributed to primary psychosis versus sepsis, although later it was felt to be likely secondary to hypocortisolism. Her acute kidney injury was deemed secondary to vascular collapse from the crisis, which rapidly improved to baseline with adequate fluid and steroid replenishment.

After being transferred to the floor from the intensive care unit, she became more alert and awake but had breakthrough episodes of combative behavior with paranoid ideations. She would often not let anyone touch her or be in her room other than her husband and son. She frequently refused to take medications when her family was unavailable, and this noncompliance exacerbated her symptoms of

delirium and psychosis. She saw rats on the walls or crawling all over her and was convinced we were trying to kill her with the medications. Her noncompliance was also associated with systolic blood pressure drops to the 90s. Family meetings were convened multiple times and the importance of not missing scheduled steroid replacement was emphasized. The family agreed to be at the bedside to enforce compliance with daily steroid dosing. After a week, her delirium and intermittent psychosis greatly improved. Her glucocorticoids were adjusted to prednisone 10mg once daily. With this, she showed considerable improvement over the next few days and was able to be discharged off antipsychotics.

DISCUSSION

Psychosis has been reported in multiple endocrine disorders, including excess cortisol in Cushing's syndrome. However, psychosis due to adrenal insufficiency from panhypopituitarism has rarely been reported in the literature and is mostly limited to individual case reports or Sheehan's syndrome.[1,2] Simultaneous thyroid under-replacement during psychotic episodes confounds the presentation as they often get mislabeled as having "myxedema madness". This was not the case in our patient as her free T4 was within normal limits.[3] Presentations are frequently similar to psychotic disorders such as schizophrenia, with symptoms including fluctuating cognition, hallucinations, delirium, persecutory delusions, and paranoid thinking. This often leads to the use of antipsychotics to treat primary psychiatric disorders.[3–5]

Partial or complete blindness in this population is also common due to damage to the optic nerve and further exacerbate symptoms.[4] Indeed, this likely partially contributed to our patient's presentation. Charles – Bonnet syndrome which causes hallucinations due to blindness should be considered as well.[6] Meanwhile, over-replacement of steroids, such as stress dose steroids during the initial presentation can cause manic symptoms or delirium, creating a see-saw effect on cognition, with both hypercortisolism and hypocortisolism presenting as altered sensorium. Other symptoms such as fatigue, nausea, hypotension, and cold intolerance are also often frequently encountered.[7] In retrospect, the causal effect of hypopituitarism and neuropsychiatric disturbances is clear, such as in our patient who promptly improved with adequate steroid replacement. This effect has been reproduced in multiple clinical settings, including primary and secondary adrenal insufficiency patients.[7,8] Unfortunately, this clinical entity seems to be poorly known throughout the medical community, including by endocrinologists.

Currently, no single explanation exists that can explain the psychiatric manifestations of hypocortisolism, although there are multiple theories. One should note that glucocorticoid receptors are abundant in the hippocampus and other areas of the brain. One study showed that acute treatment with hydrocortisone infusion (300 μg/kg/hr^{-1}) facilitated working memory concomitant with pre-frontal cortex (PFC) activation in humans. It has also been revealed that PFC cognitive deficits were induced in rats after the suppression of endogenous glucocorticoids. It was ultimately concluded that suppression of endogenous glucocorticoids was sufficient to produce PFC dysfunction and thus provided evidence that glucocorticoids are essential for maintaining PFC cognitive function.[9] Patients with Addison's disease have been shown to have abnormal EEGs, with the most frequent finding being diffuse fluctuating slow activity.[10] Meanwhile, electrolyte disturbances (frequently severe hyponatremia), hypoglycemia, and other metabolic abnormalities are often simultaneously present, which can cause encephalopathy.[10,11] Other theories include: an increased pro-inflammatory effect due to the disruption of the hypothalamic-pituitary-adrenal axis, increased neural excitability and conduction velocity along peripheral axons with simultaneous prolongation of conduction across synapses which alters signal arrival timing from the periphery to the central nervous system.[5,11] Meanwhile, there is evidence of PFC cognitive deficits such as working memory impairment in several stress-related neuropsychiatric disorders, including depression, schizophrenia, and Parkinson's disease.[9] Meanwhile, suppression of glucocorticoids induces working memory impairment through a D_1 receptor-mediated hypodopaminergic mechanism in the PFC.[9]

In patients with psychotic symptoms and panhypopituitarism, one should consider the possibility that the symptoms are secondary to low cortisol levels which may secondarily be exacerbated by other factors such as hyponatremia, hypoglycemia, and blindness. Symptoms often mimic other psychotic disorders such as schizophrenia, and practitioners should be careful before hastily making a diagnosis. Psychotic symptoms tend to rapidly resolve with glucocorticoid replacement.

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CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

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