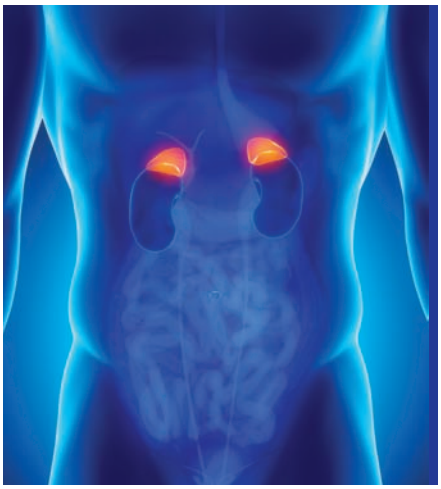

[CASE REPORT]

The Neuropsychiatric Aspect of Addison's Disease: A Case Report

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ABSTRACT

Chronic adrenal insufficiency, known as Addison's disease, presents with a constellation of symptoms and signs. The neuropsychiatric aspect of this condition is not fully understood and not much has been documented about it in the English literature. This article presents a case of a 41-year old male patient who presented initially with depression after a recent life stressor. After his condition escalated and therapy continued to fail, the medical team revised its diagnosis to Addison's disease. Neuropsychiatric symptoms could be the first presentation of Addison's disease, and thus should be kept in mind whenever such a case presents to the physician.

INTRODUCTION

Addison's disease (AD) is a medical condition characterized by chronic adrenal insufficiency leading to failure of glucocorticoid secretion.[1] Although AD has a constellation of cardinal symptoms and signs, the neuropsychiatric aspect of this condition has not been thoroughly investigated. In this report, we present a case of AD in which the patient initially demonstrated neuropsychiatric symptoms leading to a diagnosis of depression. The other symptoms typically seen in AD were not severe enough in this case to initially attract the attention of either the patient or his physicians.

CASE REPORT

A 41-year-old man who worked in construction presented to our psychiatric clinic complaining of depressed mood that started two months previously. He related his condition to the recent and violent loss of his spouse, who was killed in a car accident. The patient's symptoms included loss of concentration, lack of sleep, and loss of appetite leading to a six-pound weight loss over the previous two months. He denied any suicidal thoughts, but admitted that he sometimes heard his spouse's voice in the house. After discussing the condition as a case of depression with the patient, we started the patient on psychotherapy sessions (twice monthly) and 20mg of fluoxetine daily.

The patient came to the clinic for follow up two weeks later. He complained that the therapy had done nothing to improve his mood, and that he thought, in fact, his condition was worsening. He stated that two days previously, he thought he saw his deceased spouse in the kitchen. He also reported having thoughts about death and the futility of life without his partner, although he insisted he was not suicidal and that he had no plans for committing

suicide. We advised the patient to continue taking the fluoxetine and we increased his psychotherapy sessions to weekly. After this follow-up visit, the patient, however, only attended one psychotherapy session and was lost to follow up for several months.

Four months later, the patient presented to our emergency room (ER) with delirium, mild fever, and visual and auditory hallucinations. According to the ER team, the provisional diagnosis was substance abuse, but the toxicology screen came back negative, denying this diagnosis. The treatment team noted a weak, thready pulse, severe hypotension (70 systolic), and severe hyponatremia and hyperkalemia. A diagnosis of an Addisonian crisis was made. The patient was admitted to the intensive care unit (ICU), and proper intervention for the Addisonion crisis was administered. Later, it came to our attention that the patient had visited several physicians and hospitals in the area over the past four months, but a diagnosis of AD was not made by anyone.

DISCUSSION

AD, named after Thomas Addison, a British physician who described it in 1855, is a chronic insufficiency of the adrenal glands, leading to decreased secretion of glucocorticoids and possibly mineralocorticoids.[1] It usually presents with fatigue, weakness, abdominal pain, nausea, vomiting, weight loss, and skin hyperpigmentation.[1] An Addisonian crisis is a life-threatening condition and an absolute medical emergency. Patients suffering from an Addisonian crisis will present with severe hypotension, hyponatremia, fever, psychosis, delirium, or even coma.[1] Causes of the adrenal insufficiency include an autoimmune process or tuberculous destruction of the adrenal glands.[1] Some authors have suggested the administration of antituberculous therapy in any AD patient in developing communities.[2] Causes of *acute* adrenal insufficieny include sudden withdrawal of corticosteroid therapy and Water-House-Friderichsen syndrome, a disease of the adrenal glands most commonly caused by the bacterium *Neisseria meningitidis*.[3]

Initially, our patient presented with depressed mood as his only complaint. His depressed mood was understandable, due the presence of a recent life stressor that involved the loss of a loved one. In retrospect, the treatment team should have noted the hyperpigmentation of the patient's skin, a symptom of AD. However, the patient was very dark-skinned, and initially the treatment team attributed the hyperpigmentation to the patient's outdoor occupation in construction. The subtlety and vagueness of our patient's symptoms did not point to an underlying medical condition. In such cases where medical therapy fails to address the neuropsychiatric symptoms, the treatment team might consider a hypothyroid state, with hypothyroidism being a well-known cause of depression.[4] It is worth mentioning that hypothyrodisim can in fact co-present with AD, a condition known as Schmidt syndrome.[5]

AD from a neuropschyatric point of view. An array of neuropsychiatric symptoms is associated with AD. Addison is quoted as saying in 1855 that AD patients might present with "attacks of giddiness, anxiety in the face, and delirium."[1] Anglin et al[1] also noted four case series published in the 1940s and 1950s that found the prevalence of neuropsychiatric symptoms in AD to be between 64 and 84 percent. Iwata et al[6] reported that in some cases, the neuropsychiatric symptoms were the initial and sole presentation of AD, even though such symptoms are more common in the late course of the disease; this might lead to a patient initially being misdiagnosed, as it did in our case, and in turn, incorrectly treated. Neuropsychiatric symptoms of AD include, but are not limited to, depression, lack of energy, and sleep disturbances. During an Addisonian crisis, agitation, delirium, and, in some cases, visual and auditory hallucinations are reported.[1] According to Smart,[7] neuropsychiatric symptoms might also be the first presentation of an Addisonian crisis, especially in a patient who was previously symptom free while under therapy.

Etiological theories of neuropsychiatric symptoms. Concerning the etiology of neuropsychiatric symptoms in AD, many theories exist. Obviously, the first causes that come to mind would be the electrolytic and metabolic disturbances that are commonly associated with AD. Hyponatremia being the cardinal sign of AD could play a role in brain damage.[1,8] However, the majority of neuropsychiatric symptoms that occur in AD patients also occur in patients with normal to mildly abnormal glucose levels.[1]

In a study by Engel and Margolin,[9] attention was directed to the electrical activity of the brain, where five out of eight AD patients had abnormal electroencephalograms (EEGs). In the same study, the correlation between hypoglycemia and EEGs was observed. To be more specific, in the case report by Anglin et al,[1] the patient's initial EEG during an Addisonian crisis showed fluctuating slow activity, with 1- to 3-second bursts of slow activity, although this improved later during the patient's follow-up period.

Another hypothesis concerning the etiology of neuropsychiatric symptoms in AD would be the effect of glucocorticoids on the brain and cognitive function. Henkin[10,11] proposed that a decrease in glucocorticoids results in an increase in neural excitability, leading to an enhanced ability to detect sensory input. It has been postulated that a decrease in glucocorticoids could precipitate hallucinations as well as lower the threshold for psychosis.[1] In a more recent study by Yehuda and Seckl,[12] the authors proposed that low cortisol levels may affect vulnerability to psychopathology. This study was not on patients with

AD; however, the theory warrants more investigation nonetheless.

Corticosteroid-induced psychosis. Ironically, prolonged corticosteroid therapy, the mainstay therapy for AD patients, can cause neuropsychiatric symptoms.[13] Although many of the psychological side effects from corticosteroid use are probably of little clinical significance, some of these side effects (e.g., mood alterations, hyperactivity, insomnia, and psychosis) have been described in approximately five percent of corticosteroid-treated patients.[14] Some case reports on corticosteroid use have even described suicide attempts.[15,16] The theory that a past history of psychiatric illness is a risk factor for corticosteroid-induced psychosis is controversial, though according to a review by Patten and Neutel[17] it does not appear to impose a significant risk factor.

CONCLUSION

It is important that physicians are aware of the neuropsychiatric symptoms that can manifest in AD patients because sometimes these symptoms are the only manifestations of a life-threatening Addisonian crisis. Even if not in an emergency setting, AD should always be kept in mind while treating a psychiatric patient (especially in cases of depression and psychosis) who has no past or family history of psychiatric illness or who fails medical therapy for depression.

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