A Psychiatric Presentation of Adrenal Insufficiency: A Case Report

To the Editor: Adrenal insufficiency has been shown to display a wealth of possible psychiatric presentations including psychosis, depression, anxiety, mania, and cognitive impairment, alongside the known vague physical symptoms.[1] Adrenal insufficiency is notoriously challenging to diagnose, with up to 60% of patients having been seen by at least 2 clinicians prior to diagnosis and a median duration to diagnosis of up to 2 years.[2] These psychiatric symptoms may even present with no physical symptoms.[1]

There are several known causes of secondary adrenal insufficiency, although it is most commonly associated with an abrupt disruption in prescribed corticosteroid therapy (such as during an emergency hospital admission). Another less-often considered and rarer cause for secondary adrenal insufficiency is use of opiate medication, a commonly prescribed class of painkillers in both hospital and general practice settings. Opiates can cause hypothalamic suppression of corticotrophin-release hormone and, therefore, adrenocorticotropic hormone (ACTH) with resultant adrenal atrophy.[3]

In fact, while "opiate endocrinopathy" has earned increasing interest in the literature as a potential side effect of long-term or high-dose opiate use,[3] only a handful of case reports[4,5] describe opiate-induced secondary adrenal insufficiency, and none describe a solely psychiatric presentation.

Guidelines for the management of depression from the National Institute for Clinical Excellence[6] in the United Kingdom currently only contain information on the recognition and management of low mood symptoms, with no guidance for the screening of their many potential physical causes. With our increasing understanding of the fine interplay between physical disease and mental health, this guidance is potentially outdated. This case highlights the need to rule out physical causes even for patients with long-standing psychiatric diagnoses, as often the line between physical and mental health can be so blurred that careful investigation is important to avoid either potentially life-threatening complications or incorrect and ineffective treatment regimens.

Case report. Mr A, a 32-year-old man with a 6-year history of poorly controlled depression and nonspecific anxiety disorder, was admitted in February 2014 to the assessment ward of a busy mental health unit in South Wales, United Kingdom, with a 1-day history of distressing and persecutory auditory hallucinations, paranoid delusions, and polydipsia. A urine drug screen was positive for amphetamines, benzodiazepines, and opiates; the latter 2 were most likely related to prescribed medication. Treatment was commenced accordingly with low-dose quetiapine. The symptomatology improved quickly, and a diagnosis of drug-induced psychosis (*DSM-IV* criteria) was made.

The drug and alcohol services team was familiar with Mr A, as he had a long-standing history of opiate dependence for pain relief after a road traffic accident 8 years prior. He now takes buprenorphine replacement. His long-standing symptoms of low mood, poor concentration, poor sleep, and low energy have affected his education, work, and personal life for several years. For a 6-year period, he has received trials of numerous antidepressants including citalopram, sertraline, fluoxetine, venlafaxine, and mirtazapine with no long-term improvement. Mr A has a strong family history of mental health disorder; his maternal mother and grandmother suffer from depression and his maternal aunt has bipolar affective disorder.

During the hospital admission, Mr A's laboratory test results were reviewed historically and revealed persistent, uninvestigated mild hyponatremia (2–3 mmol/L) of several years' duration. Results of other laboratory investigations and imaging were normal (Table 1). While polydipsia might account for his serum sodium changes, an undetectable random cortisol level was found, alluding to a potential cause for his psychiatric and laboratory test findings. An intravenously administered short Synacthen test revealed an inappropriate cortisol response with a low-normal ACTH level, confirming secondary adrenal insufficiency (see Table 1), with his opiate-replacement medication identified as the most likely cause. Mr A was transferred to the endocrine team to begin corticosteroid replacement therapy. There were no complaints of weight loss or gain by Mr A prior to or during the admission, and his blood pressure remained stable.

Following commencement of corticosteroid replacement therapy, Mr A's biochemical results normalized and his mental state improved. Mr A now reports a sustained improvement in mood and concentration and no further psychotic symptoms. His family states that he is spending more time out of the house with friends and has begun to take steps to seek employment. The plan is to gradually wean Mr A off psychiatric medication with a view to ascertaining whether these markedly positive changes are indeed related to corticosteroid replacement therapy.

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Table 1. Mr A's Laboratory Test Results

Test	September 2012	May 2013	April 2014	May 2014	May 2014	June 2014	June 2014	Reference Range
Sodium, mmol/L	132	131	133	126	127	138	140	135–145
Potassium, mmol/L	4.3	4.4	4.3	4.4	4.2	3.9	4.0	3.5–5.0
Urea, mmol/L	1.1	2.4	2.8	2.2	2.6	4.1	4.0	2.5–7.8
Creatinine, mmol/L	76	78	71	72	77	80	79	58–110
Random glucose, mmol/L	…	4.1	…	3.7	3.9	6.5	7.1	4.4–9.8

Cortisol basal sample	< 25	(171–536 nmol/L)
Corisol 30 min postsynthetic ACTH	103	
ACTH	18.7	(7.2–47 ng/L)

Abbreviation: ACTH = adrenocorticotropic hormone.

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Published online: October 29, 2015.

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Potential conflicts of interest: None reported.

Funding/support: None reported.

Previous presentation: This case report was presented at a local educational meeting at University Hospital of Wales; November 12, 2014; Cardiff, United Kingdom.

Acknowledgment: The author thanks Sharmila J. Menon, MBBS, MBA, MRCPsych, MSc, consultant psychiatrist, and Kishore T. Kale, MBBS, MD, MRCPsych, consultant psychiatrist, Cwm Taf University Health Board, Royal Glamorgan Hospital, South Wales, United Kingdom. Drs Menon and Kale report no conflicts of interest related to the subject of this letter.

Prim Care Companion CNS Disord 2015;17(5):doi:10.4088/PCC.15l01819

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