

## Non-Acute Transient Reversible Adrenal Insufficiency in a Survivor of Critical Illness: A Lesser-Known Cause of Primary Adrenal Insufficiency

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### Abstract:

*Objectives:* Primary adrenal insufficiency AI is regarded as a progressive disease needing lifelong replacement therapy, but this may not always be the case.

*Material and methods:* A non-acute presentation of AI following a hypotensive episode caused by blood loss was investigated.

*Results:* Adrenal function fully recovered without treatment.

*Conclusions:* There should be a high index of suspicion and a low threshold for performing tests of adrenal function in survivors of critical illness and severe hypotensive episodes.

**Keywords:** Adrenal insufficiency, transient adrenal ischaemia, reversible adrenal dysfunction

**Received:** 12/06/2014

**Accepted:** 23/07/2014

**Published:** 28/07/2014

**How to cite this article:** Chandrasekeram S, Parker R, Mudenha E, Fernando DJS. Non-Acute Transient Reversible Adrenal Insufficiency in a Survivor of Critical Illness: A Lesser-Known Cause of Primary Adrenal Insufficiency, *EJCRIM* 2014;**1**:doi:10.12890/2014\_000098

**Conflicts of Interests:** The authors declare that they have no conflicts of interest in this research.

## Introduction

The diagnosis of primary adrenal insufficiency (AI) is not synonymous with the label of Addison's disease. However, Addison's disease caused by autoimmune adrenalitis remains by far the most common cause of primary AI. The prevalence of primary AI is reported to be 93–140 per million and secondary insufficiency has a prevalence of 125–280 per million[1].

Primary AI caused by autoimmune adrenalitis leading to Addison's disease is regarded as a progressive disease needing lifelong glucocorticoid and mineralocorticoid replacement therapy. However, a single case report documents partial recovery from autoimmune primary AI[2]. Hence AI may not always be an incurable disease with a need for life-long steroid replacement therapy.

Acute primary AI and acute secondary AI have also been reported following shock after a surgical procedure or trauma[3]. Changes implicating AI as a cause of death or co-morbidity have also been documented in post mortem findings[4]. AI has also been reported after cardiac arrest, but its prognostic significance and the value of pre-emptive intervention are unclear[5].

Post-operative or critical illness-related primary AI has been reported as having an acute onset in adrenal crisis and as being persistent[3-5]. A chronic or sub-acute presentation does not appear to be common.

We report the case of a non-acute presentation of AI following a hypotensive episode caused by blood loss with subsequent full recovery of adrenal function.

## Case report

A 38-year-old woman was referred to the endocrine service as she was tired and her family doctor could not identify a cause apart from low cortisol. Her symptoms were of progressively increasing tiredness. She had no postural symptoms. She was known to have experienced a significant period of post-operative prolonged hypotension 4 months before presentation. At presentation to the endocrinology service, physical examination was unremarkable and she had no physical signs to suggest an endocrine illness. Haematological and biochemical indices were all within reference ranges. Prolactin was 326, LH 4.6, FSH 5.0 and ACTH 18 (08:40 h). She had a sub-optimal cortisol response to stimulation with tetracosactrin (*Table 1*). Adrenal antibodies were negative. The diagnosis was diminished adrenal reserve due to primary AI but unlikely to be caused by autoimmune adrenalitis. In the absence of evidence to suggest other causes of primary AI, the most likely cause was thought to be post-hypotensive AI.

Time	0	Week 6	Week 12	Week 18
0	193	178	394	376
30 min	408	529	624	738

*Table 1 Results of corticotrophin stimulation test*

The diagnosis was discussed with the patient and surgeons. The patient wished to avoid replacement therapy with steroids. She received sick day rule advice as for primary AI and was given a stock of steroids for use in an emergency and emergency contact numbers but did not receive replacement therapy. Further elective surgery was deferred pending resolution of her adrenal function. She underwent serial corticotropin stimulation tests, which showed improving adrenal response leading to full recovery. She later underwent an elective surgical procedure without steroid cover uneventfully with no haemodynamic instability during or after surgery.

### **Discussion**

Our patient's findings suggest that some patients may progress to have absolute AI with a prolonged period of recovery which may not have been evident in previous intensive therapy unit-based case series as they were not designed to assess long-term effects on hypothalamic-pituitary-adrenal (HPA) function.

Our patient's presentation was unusual in that it was of a more insidious nature mimicking that of autoimmune adrenalitis. However, in the absence of antibodies, co-existence of other autoimmune disease and the occurrence following massive blood loss suggest that the mechanism of causation was hypotension and ischaemia of the adrenal glands, although adrenal haemorrhage cannot be ruled out as imaging was carried out some time after the acute insult and in the recovery phase. The absence of clinical signs and biochemical evidence of other pituitary dysfunction and the presence of detectable ACTH suggests primary AI although we did not perform a CRH test or dynamic pituitary function tests to establish normal pituitary reserve.

Our patient's symptoms were non-specific and she did not have the classic signs of primary AI such as pigmentation and postural hypotension although she did have tiredness. We conclude that symptoms of AI following critical illness may be missed as they may be attributed to anaemia, post-operative symptoms or the effects of post-traumatic stress disorder following life-threatening critical illness. Transient reversible AI may be more common than previously thought as it may present without adrenal crisis.

Our case shows that such patients may have a non-acute presentation. The identification of potential risk factors such as recent critical illness, shock, sepsis or blood loss should be an integral part of the investigation of suspected AI, which should be considered as a diagnosis if other causes seem unlikely. Furthermore, there may be a case for extending traditional studies of adrenal function in patients treated in critical care units to study the long-term effects of adrenal function in survivors of critical illness and severe hypotensive episodes. Until reliable data are available, treatment plans should take into account individual circumstances and patient preference stated as an informed empowered choice.

### Learning Points

- Symptoms of adrenal insufficiency (AI) following critical illness may be missed as they may be attributed to anaemia, post-operative symptoms or the effects of post-traumatic stress disorder following life-threatening critical illness.
- Transient reversible AI may present without adrenal crisis.
- The identification of potential risk factors such as recent critical illness, shock, sepsis or blood loss should be an integral part of the investigation of suspected AI, which should be considered as a diagnosis if other causes seem unlikely.

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