Addisonian crisis presenting with a normal short tetracosactrin stimulation test

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Summary: We report the case of a 70 year old man who presented with physical and biochemical features suggestive of Addison's disease, but had a normal short tetracosactrin (Synacthen) test. Six months later he re-presented with similar clinical features but with an abnormal response to tetracosactrin confirming the diagnosis of Addison's disease. We recommend that if adrenal insufficiency is strongly suggested further investigation should be performed to exclude this diagnosis.

Introduction

The 30 minute tetracosactrin test ('short Synacthen test') first described in 1965,1 is widely used to confirm a clinical diagnosis of Addison's disease; its use has also extended to the diagnosis of secondary adrenocortical failure.2 Its sensitivity is such that it is recommended as the only screening test necessary to make this diagnosis. We report a patient presenting with suspected Addisonian crisis, who had a normal short Synacthen test, but 6 months later had a similar clinical presentation accompanied by an abnormal short Synacthen test.

Case report

A 70 year old man presented with a 5 day history of epigastric pain and vomiting. He was not on regular medication and was previously fit, apart from two episodes of vomiting, diarrhoea and dehydration, for which he had briefly been admitted to other hospitals over the preceding 2 years and from which he had promptly recovered. He appeared unwell with a pulse of 90 beats/min, blood pressure (BP) of 120/70 mmHg, normal pigmentation, and an otherwise normal examination. Serum biochemistry at this time showed sodium 121 mmol/l, potassium 5.3 mmol/l, urea 9.0 mmol/l and creatinine 89 μmol/l, and the possible diagnosis of Addison's disease was suggested. He was initially treated with intravenous saline, and subsequently a short Synacthen test was performed. However, the diagnosis of Addison's disease was thought to have been excluded as a result of a normal 60 minute response to 250 μg tetracosactrin. Pre-dose cortisol was 307/nmol/l, and at 60 minutes 645 nmol/l. Adrenocorticotrophic hormone (ACTH) concentration at this time was 220 ng/l (range 10–80). Following intravenous rehydration with saline, the patient's symptoms were relieved and he was allowed home. No further investigation was undertaken at this point, and subsequent follow-up saw him well 4 months later with normal biochemistry and he was discharged.

Six months later he re-presented with a 5 day history of vomiting, anorexia, general weakness and lethargy. He had been fit and well since the similar episode 6 months before. Examination showed him to be unwell, dehydrated, with normal pigmentation and secondary sex characteristics. His pulse was regular at 90 beats/min, BP 75/40 mmHg (supine), 60/30 mmHg (erect). The examination was otherwise normal. Initial investigations showed a haemoglobin of 17.0 g/dl, white cell count of 5.2 × 10^9/l, sodium 116 mmol/l, potassium 5.2 mmol/l, urea 14.6 mmol/l, creatinine 132 μmol/l, albumin 48 g/l and calcium 2.52 mmol/l. Serum cortisol at the time of presentation was 320 nmol/l and 60 minutes after 250 μg tetracosactrin was 280 nmol/l (performed before the initiation of any treatment). Aldosterone concentration was 80 pmol/l (range 100–450). Adrenal antibodies were negative and there was no calcification in the adrenals, confirmed by computed tomographic scan. The patient was treated initially with saline and hydrocortisone and he made a good recovery – he was subsequently changed to oral hydrocortisone and fludrocortisone, his blood pressure and biochemistry returned to normal and he was allowed home.

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Accepted: 28 October 1991
Discussion

It is widely accepted that a normal response to tetracosactrin excludes the diagnosis of Addison's disease. This was clearly not the case in the patient described. A number of cases have been described of patients with anti-adrenal antibodies, with initially normal tetracosactrin responses who have been followed up over several years – and who after initially having normal responses to tetracosactrin subsequently developed abnormal responses.4 However, these patients all had polyglandular autoimmune failure and were all asymptomatic with regard to their Addison's disease. Zona glomerulosa failure and abnormal biochemistry, in a teenager with polyglandular autoimmune failure and cutaneous candidiasis, has also been reported, 4 years prior to the development of an abnormal response of cortisol to tetracosactrin stimulation.5 We have been unable to find any similar reports.

The elevated ACTH (220 ng/l) at the initial presentation in our patient might have prompted further investigation. However, serum concentrations of 290–3,900 ng/l (mean 1,001 ng/l) were reported in a series of patients with Addison's disease, all above the level seen in our patient.6

We surmise that at the time of initial presentation our patient had a mineralocorticoid deficiency, but only subsequently developed glucocorticoid failure, accounting for the normal response to tetracosactrin in the short Synacthen test, and subsequent delay in the diagnosis of Addison's disease. We reiterate that if there is a strong clinical suspicion of Addison's disease, the short Synacthen test should be performed immediately, prior to treatment. If there is a normal response to tetracosactrin, further investigation with serum aldosterone and renin estimations should be performed to assess mineralocorticoid function, before the diagnosis is excluded.

References

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doi: 10.1136/pgmj.68.800.465

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