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Research Article

Cytomegalovirus (CMV) Adrenalitis Leading to Adrenal Insufficiency in a Patient with AIDS, Disguised by Concomitant Corticosteroid Administration: A Case Report

Authors

Sonakshi Sharma and Ian Holdaway

Endocrinology Registrar, Department of Endocrinology, Greenlane Clinical Centre, Auckland, New Zealand

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Abstract

Background: Recognition of Cytomegalovirus related primary adrenal insufficiency in patients with Acquired Immunodeficiency Syndrome (AIDS) requires a high clinical suspicion in patients already on glucocorticoids, especially if the glucocorticoids are to be withdrawn. **Case Presentation:** We report the case of a 67 year old man with a new diagnosis of Human immunodeficiency virus and multiple AIDS defining illnesses including disseminated Cytomegalovirus infection. The use of six weeks of prednisone therapy for an exacerbation of chronic obstructive pulmonary disease resulted in a delay in the diagnosis of primary adrenal insufficiency from Cytomegalovirus in this patient resulting in marked hypoadrenal symptoms when prednisone therapy was stopped. **Conclusion:** Our case

highlights the importance of investigating for adrenal insufficiency in patients with Cytomegalovirus adrenalitis, regardless of prior or concurrent treatment with glucocorticoids, particularly if glucocorticoids are to be withdrawn.

Keywords: HIV/AIDS, Cytomegalovirus, adrenal insufficiency, glucocorticoids

Introduction

The adrenal gland is the most commonly involved endocrine organ in autopsy studies of patients who die of Acquired Immunodeficiency Syndrome (AIDS) (Welch 1984). The most common finding at autopsy is the presence of intranuclear or intracytoplasmic inclusion bodies in enlarged adrenal cells,

indicative of Cytomegalovirus (CMV) adrenalitis (Eledrisi & Vergheze 2001). Despite the frequent involvement of the adrenal glands with CMV, overt adrenal insufficiency is uncommon in these patients. This is because at least 80% of the gland must be destroyed before adrenal insufficiency becomes clinically apparent and requires treatment (Hofbauer & Heufelder, 1996; Grinspoon & Bilezikian, 1992). We report a case where the diagnosis of hypoadrenalism was further delayed because the patient had recently been treated with corticosteroids.

Case Presentation

A 67 year old bisexual man was admitted to hospital with cough, fever, weight loss and oral thrush coming on over several months before admission. His recent Human Immunodeficiency Virus

(HIV) test in the community was positive. His absolute CD4 count was 11 cells per μl on admission with a HIV viral load of 454,528 copies/ml. He was mildly hyponatremic on admission with a serum sodium of 134 mmol/L, (normal 135-145) which persisted throughout most of his hospital stay with measurements mainly ranging from 127 to 134 mmol/l. His serum potassium over this time ranged from 4.1 to 5.6 mmol/l (normal 3.5-5.5). His initial morning cortisol was 367 nmol/L (normal range 200-700) and his hyponatremia was thought by the Infectious Diseases team caring for him to be secondary to the syndrome of inappropriate ADH secretion (SIADH).

His CT chest showed patchy ground-glass opacification and his sputum immunofluorescent stain was positive for *Pneumocystis Jirovecii*. He was diagnosed with *Pneumocystis pneumonia* and

was commenced on a high dose of Cotrimoxazole. Due to ongoing febrile episodes and wasting, he was started on anti-retroviral therapy with Raltegravir, Tenofovir, and Emtricitabine. His diarrhoea and loss of appetite was investigated with a colonoscopy and a biopsy of the descending colon showed intranuclear and intracytoplasmic inclusion bodies consistent with CMV infection. A gastroscopy was diagnostic of CMV esophagitis and gastritis. CMV PCR in all the bowel specimens was positive and plasma CMV viral load was 27,116 IU/ml. He was commenced on Valganciclovir, which was stopped after one month. He subsequently developed visual blurring and was diagnosed with CMV retinitis complicated by haemorrhage. He was treated with intravitreal foscarnet and was restarted on oral valganciclovir. His Quantiferon Gold test for tuberculosis was negative.

He was noted on the ward to be short of breath and hypotensive with a systolic blood pressure of 80 mmHg. This was thought to be due to heart failure secondary to a myocardial infarction, as well as an exacerbation of chronic obstructive pulmonary disease due to past cigarette use. He was commenced on 40 mg of prednisone daily, and this was slowly weaned over six weeks. His systolic blood pressure was 100mmHg while on a reducing dose of prednisone. His electrolytes showed ongoing hyponatremia and intermittent hyperkalemia while on prednisone. One week after stopping prednisone, he became markedly hypotensive with systolic blood pressure of 80 mmHg and worsening hyponatremia (120 mmol/L) with hyperkalemia of 5.8 mmol/L (normal 3.5-5.5). He developed nausea at the time of hypotension, but there was no history of vomiting or abdominal pain. A 250 µg short synacthen stimulation test showed a

suboptimal rise in serum cortisol from 225 nmol/L to 265 nmol/L (normal response >500nmol/l). His plasma ACTH was at the upper limit of normal at 11 pmol/L (normal 2-11). He was thought by the attending Infectious Diseases team to have secondary adrenal suppression from the recent prednisone treatment. His retroviral therapy was not thought to be contributing to the abnormal adrenal function. He was recommenced on prednisone 5 mg daily, and his systolic blood pressure improved to 100 mmHg.

He was seen for the first time in the Endocrinology clinic two weeks after hospital discharge and was noted to be hyperpigmented with a low blood pressure of 90/70 mmHg lying and a significant symptomatic postural drop to 75/60mmHg on standing. Repeated hormonal testing prior to his morning dose of

prednisone showed a 0900hr serum cortisol of 90 nmol/L, ACTH 33 pmol/L, aldosterone 266 pmol/L (normal 60-1000) and plasma renin 83 mU/L (normal 4-46). A CT scan of his adrenal glands showed new bilateral adrenal atrophy compared to a scan performed five months previously. He was commenced on Fludrocortisone 0.1 mg daily with marked improvement in his symptoms of fatigue and dizziness and normalization of his blood pressure and electrolytes.

Discussion

The differential diagnosis of primary adrenal insufficiency in this patient includes autoimmune, fungal or viral aetiology. His Quantiferon Gold test for Tuberculosis was negative and his bronchoscopy samples showed no signs suggestive of

Tuberculosis. His adrenal autoantibodies were also negative. His primary adrenal insufficiency was most likely due to disseminated CMV infection resulting in adrenalitis. He was noted to be hyponatremic on admission with intermittent episodes of hyperkalemia during his inpatient stay. Interestingly, his electrolyte abnormalities did not improve while he was on treatment with Prednisone, presumably due to lack of mineralocorticoid replacement and his systolic blood pressure was never greater than 100 mmHg. However, his symptoms, blood pressure and electrolytes normalised immediately after addition of fludrocortisone replacement treatment. Prior use of prednisone thus resulted in a nearly seven week delay in the diagnosis of primary adrenal insufficiency, with dangerously low blood pressure and major hyponatremia when off corticosteroid replacement. This was initially diagnosed by the team caring for

him as being due to suppression of the hypothalamic pituitary adrenal (HPA) axis from the prior prednisone treatment, which had caused a low level of ACTH, leading to an incorrect diagnosis of secondary adrenal insufficiency.

Our case indicates that clinicians should have a high index of suspicion for adrenal insufficiency in patients with disseminated CMV infection. CMV has been demonstrated at autopsy in the adrenal glands of 40-88% of patients who die of AIDS (Glasgow et al. 1985; Sellmeyer & Grunfeld 1996). As the extent of adrenal necrosis due to CMV infection does not usually exceed 50-60% of the total parenchyma, CMV causes adrenal insufficiency in only 3% of patients with AIDS (Glasgow et al. 1985; McKenzie 1991; Sellmeyer & Grunfeld 1996). The presence of CMV retinitis or CMV antigen positivity has been shown to independently serve as

marker for possible adrenal dysfunction in AIDS patients (Hoshino et al. 1997). It is prudent to investigate for adrenal insufficiency in patients with these abnormalities, regardless of prior or concurrent treatment with glucocorticoids, particularly if glucocorticoids are to be withdrawn. This also applies to patients with hypotension or electrolyte abnormalities while on treatment with a relatively pure glucocorticoid such as prednisone. Importantly, CMV- related adrenal insufficiency in AIDS has also been reported to occur in patients who are on supraphysiological doses of corticosteroids for treatment of pneumocystis pneumonia, but in the absence of CMV retinitis (Razzaq et al. 2002). Such patients often present similarly to our patient with other clues of adrenal insufficiency, such as refractory hypotension, hyponatremia, hyperkalemia and fatigue despite

prednisone use, due to the minimal mineralocorticoid activity of prednisone.

The diagnosis of primary adrenal insufficiency in those under treatment with corticosteroids for other conditions remains challenging. However, as in our patient, most individuals will show the typical features of low serum cortisol and raised plasma ACTH in the morning prior to the administration of their usual glucocorticoid therapy (Arlt & Allolio 2003). Exceptions can occur if the dose of corticosteroid is markedly supraphysiological, and in these cases retesting after slow decrease in corticosteroid dosage may be needed.

Conclusion

The diagnosis of primary adrenal deficiency in patients with CMV adrenalitis on concurrent glucocorticoid therapy is clinically important to avoid potential collapse from hypoadrenalism following glucocorticoid withdrawal, and to avoid ongoing symptoms in those on lower doses of corticosteroids who are not replaced with mineralocorticoid treatment.

Consent

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

List Of Abbreviations

CMV: Cytomegatovirus

AIDS: Acquired Immunodeficiency Syndrome

HIV: Human Immunodeficiency Virus

HPA: Hypothalamic pituitary adrenal

Competing Interests

There are no competing interests to declare in relation to this manuscript.

Author Contribution

SS: Reviewed the patient clinically, summarized the data, performed a literature review and drafted the manuscript.

IH: Revised the manuscript critically for important intellectual content and gave final approval of the version to be published.

All authors read and approved the final manuscript.

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