# A Rare Case of Autoimmune Addison's Disease in a Patient with Previously Diagnosed Primary Hyperaldosteronism

Sir,

We describe the case of a 79-year-old lady who presented in 1999 to her GP with refractory hypertension (initial blood pressure [BP] was 210/135 mmHg) associated with unexplained hypokalaemia. A review of her records showed that she had evidence of hypokalaemia since 1994. She was otherwise well and active with insignificant past medical and family history. She denied consuming any liquorice. The GP treated her initially with amlodipine and lisinopril was added later in view of hypokalaemia, along with oral potassium supplement and referred to endocrine team for further assessment.

On initial assessment, her BP was 185/110 mmHg with body weight of 68 kg (BMI 22 kg/m$^2$) and systemic examination was normal. In the view of her history, she was investigated for primary aldosteronism (PA) which was confirmed biochemically (results are mentioned in Table 1), hence started on spironolactone 50 mg/day initially. As per the endocrine society guideline,[1] in the setting of spontaneous hypokalaemia, plasma renin below detection levels plus plasma aldosterone concentration more than 550 pmol/L, no further confirmatory testing is needed. She had a CT abdomen (in 2001) which did not reveal any adrenal mass or hyperplasia. As the patient did not wish to consider surgery, adrenal venous sampling (AVS) was not pursued and she continued on long-term spironolactone. As there was no indication for genetic testing, it was not done.

In June 2016, the patient presented to the emergency department with a fall and complained of lethargy, worsening fatigue and postural dizziness. A month prior to this, she was admitted to hospital and treated as vasovagal syncope with hyponatraemia (her sodium was 121 mmol/L and potassium was 4.5 mmol/L on admission) due to dehydration and her Spironolactone was stopped at that time.

On clinical examination, there was postural hypotension. She also appeared tanned despite denying excessive exposure to the sun. The rest of the systemic examination was normal.

Initial investigations showed hyponatraemia and hyperkalaemia (Na: 108 mmol/L and K: 6.4 mmol/L) which raised the concern that she might have developed adrenal insufficiency which was later confirmed by a short synacthen test [Table 2]. Further biochemical workup revealed positive adrenal antibodies, low aldosterone-to-renin ratio with a high adrenocorticotropic hormone level that further secured the diagnosis of new-onset Addison's disease (AD) [Table 2]. She also had an MRI scan of the adrenal glands which was normal. She was started on hydrocortisone and fludrocortisone replacement with good clinical and biochemical response [Figure 1].

**Table 1: Initial investigations done in the period from October 1998 up to 2004**

| Parameters (reference range) | 10/1998 | 08/1999 | 03/2000* | 07/2004* |
|---|---|---|---|---|
| Sodium (134–147) mmol/L | 143 | 144 | 140 | 140 |
| Potassium (3.5–5) mmol/L | 2.9 | 3.4 | 4 | 4.4 |
| Bicarbonate (19–29) mmol/L | 31 | 28 | | |
| Urea (2.5–7) mmol/L | 3.7 | 4.8 | 5.1 | 7.1 |
| Creatinine (50–120) µmol/L | 52 | 64 | 96 | 100 |
| *Patient was on Spironolactone from the point of diagnosis until 2016 | | | | |
| Initial tests | Aldosterone* (supine: 103–859) | | | 625 |
| AUG 1999 | (Ambulant: 103–1197) pmol/L | | | |
| | *Measured using Siemens Coat-a-Count RIA | | | |
| | Renin* | | | <0.2 (Suppressed) |
| | Recumbent: 1.1–2.7 ng/mL/h | | | |
| | Upright: 2.8–4.5 ng/mL/h | | | |
| | *Diasorin RIA | | | |
| | Aldosterone/Renin ratio (ARR) | | | >3000 (High) |
| | (cut-off 1000 pmol/ng/mL/h) | | | |
| | 24 h urinary Aldosterone | | | 89 nmol/24 hours (High) |
| | (10–50 nmol/24 h) | | | |
| | 24 h urinary potassium | | | 64 mmol/L |
| | 24 h urinary sodium | | | 103 mmol/L |
| | TSH (0.3–4.0 mU/L) | | | 2.48 mU/L |
| | Magnesium (0.7–1.0) | | | 0.83 mmol/L |

**Table 2: Investigations done in 2016 when the patient was diagnosed with adrenal insufficiency**

| Parameters (reference range) | 06/2016 | 08/2016* |
|---|---|---|
| Sodium (134–147) mmol/L | 108 | 129 |
| Potassium (3.5–5.3) mmol/L | 6.4 | 4.2 |
| Urea (2.5–7.0) mmol/L | 7.3 | 7.2 |
| Creatinine (50–120) µmol/L | 84 | 88 |
| eGFR (>90 mL/min/1.73 m²) | 57 | 54 |
| *After starting on steroid | | |
| 06/2016 results | | |
| Aldosterone* | <103 | |
| (supine: 103–859) | | |
| (Ambulant: 103–1197) pmol/L | | |
| *Measured using IDS ISYS assay (chemiluminescent immunoassay) | | |
| Renin (Supine: <59.7) | 47.8 | |
| (Ambulant: 5.3–99.1) mIU/L | | |
| Aldosterone/Renin ratio in pmol/mIU (cut-off 30) | <3 | |
| ACTH (<47 ng/L) | 351 | |
| SST (failed) | Cortisol (nmol/L) | |
| 0 min | 201 | |
| 30 min | 201 | |
| 60 min | 234 | |
| Adrenal auto-antibodies | Positive | |
| MRI adrenal | Normal | |

ACTH: Adrenocorticotropic hormone, SST: Short synacthen test

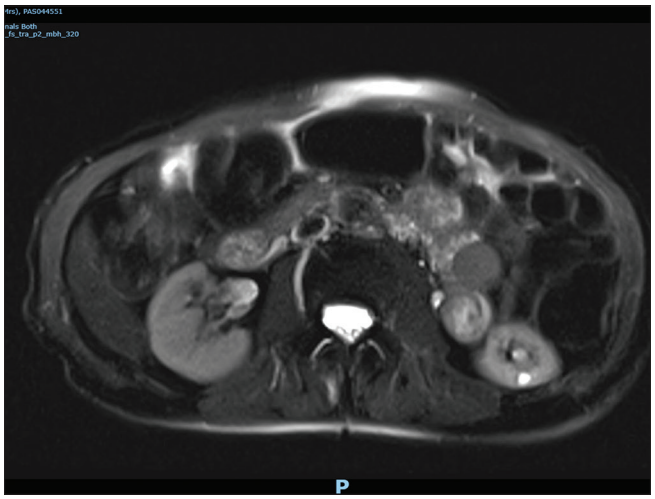

**Figure 1:** MRI adrenal (axial view)

Reviewing the literature, no case has been documented, mentioning of any new-onset AD in a patient with a confirmed PA. Few case reports have been published in the past describing remission of PA after prolonged treatment with mineralocorticoid antagonist, which were mainly reported in patients with bilateral adrenal hyperplasia.[2]

A review of the study population by Fischer and colleagues in the German Conn's registry[3] revealed that 2 of 37 (5.4%) patients had spontaneous remission, where the mean period of mineralocorticoid antagonist treatment was 5.8 ± 0.7 years. Also, another case report[4] describes a patient with known PA, who developed secondary adrenal insufficiency following ruptured aortic aneurysm.

In summary, the occurrence of AD in a previously confirmed PA is a rare unusual condition but possible, although we have no current data to predict which patients are more likely to develop that, hence follow-up of patients with such long-term condition remains paramount and periodical diagnostic assessment is justified in selected patients, when needed.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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