Our third case demonstrates that, if WISN does occur, prompt initiation of remedial therapy may prevent the development of permanent tissue damage. Initial appearances

may mimic those of a haematoma (a much more common complication of warfarin therapy) and a high index of suspicion is needed.

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Calcium-channel blockade can mask the diagnosis of Conn's syndrome

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Summary

A 30-year-old woman presented with hypertension and hypokalaemia, and was found to have primary aldosteronism due to a Conn's adenoma, whose removal cured the hypertension. Before surgery, the characteristic biochemical changes which enabled the diagnosis were completely masked by administration of a calcium-channel blocker, amlodipine. It is likely that widespread use of this class of drugs contributes to under-diagnosis of Conn's syndrome as a curable cause of hypertension.

Keywords: Conn's syndrome; aldosterone; calcium blockade

Since its first recognition, the prevalence of primary hyperaldosteronism, or Conn's syndrome, as a cause of hypertension has been disputed. Initial optimism that 20% of hypertensives may have a curable cause gave way to a realisation that many patients with essential hypertension have low renin hypertension, and nowadays less than 1% of patients started on treatment for hypertension are considered to have the diagnosis. Recently, systematic surveys using a ratio of aldosterone to renin above 800 as an upper limit of normal have suggested prevalence figures greater than 10% (of hypertensives).¹ Ironically, changes in modern pharmacological treatment of hypertension have probably reduced the sensitivity of plasma electrolyte measurements for detection of Conn's syndrome, since the 4–8-fold lower doses of diuretics – and lower overall use of this class – than in Conn's time means that plasma K^+ values <3 mmol/l are seen infrequently; it is also likely that reductions in average salt intake limit the degree of hypokalaemia in Conn's syndrome. Both sodium and diuretic intake influence how much K^+ is lost through K^+/Na^+ exchange in the renal distal tubule. Angiotensin-converting enzyme (ACE) inhibitors suppress angiotensin-II-mediated aldosterone secretion. Suppression of aldosterone release from adrenal zona glomerulosa cells by Ca^{++} entry blockers is well described,^{2,3} but their effect in Conn's syndrome has been controversial.^{4,5} While the specific antagonist for aldosterone, spironolactone, is known sometimes to confuse diagnosis of an adenoma

Figure Effects of treatment on plasma K^+ and aldosterone levels in a patient with Conn's syndrome. Plasma K^+ (—○—, left axis) and aldosterone (---□---, right axis) were measured before any treatment, and 4 weeks after the drug or surgical interventions shown on the x-axis.

by masking suppression of the contralateral adrenal, there is no generally recognised recommendation to withdraw Ca^{++} blockers during investigation of possible Conn's syndrome; there is also no published experience with amlodipine, arguably the most powerful and now most widely used member of the class in hypertension. We therefore report here a patient with a Conn's adenoma in whom serial K^+ and aldosterone measurements demonstrated how treatment with amlodipine can completely mask the diagnosis.

A previously asymptomatic 30-year-old doctor's wife was found to have a blood pressure of 160/110 mmHg at her general practice new patient medical. Plasma electrolytes showed a Na^+ of 144 and K^+ of 2.8 mmol/l, and the patient was referred untreated for further investigation. A low plasma renin (<0.2 pmol/ml/h) and elevated plasma aldosterone (730 pmol/l) suggested a diagnosis of Conn's syndrome. Onset of early morning headaches necessitated some antihypertensive treatment, and the patient was started on amlodipine 5 mg daily since premature use of spironolactone can confuse tests to distinguish adenomas from bilateral hyperplasia. Two weeks later, blood pressure had fallen to 110/70 mmHg, and the diagnosis of a right adrenal adenoma was made by computed tomography (CT) scan, and unilateral increased uptake of selenium cholesthenol by the right adrenal on scintiscan. At this stage, treatment was changed from amlodipine to spironolactone, with continued excellent blood pressure control. A 2×1 cm adrenal adenoma was removed one month later.

The figure shows the changes in plasma K^+ and aldosterone in response to each change in treatment. At least two K^+ measurements were made during each phase, with all the pairs being similar except for the spontaneous variation in K^+ before treatment was started. Unexpectedly, plasma K^+ was >4.0 mmol/l on each occasion after introduction of amlodipine, almost certainly due to a suppression of aldosterone secretion. Indeed the fall in plasma aldosterone is all the more impressive in that a

Learning points

- the diagnosis of Conn's syndrome should be suspected in any hypertensive patient with a plasma $\text{Na}^+ >140$ mmol/l, whose plasma K^+ is below the local laboratory's normal range
- the diagnosis of Conn's syndrome is then readily confirmed by demonstration of an elevated aldosterone to renin ratio (usually >800)
- administration of a calcium channel blocker, now estimated to be part of the treatment of 25% of hypertensive patients, can completely suppress both the elevated aldosterone secretion and consequent hypokalaemia. Therefore, the diagnosis of Conn's syndrome may be neither suspected or confirmed in such patients

rise in plasma K^+ usually stimulates aldosterone secretion.

Discussion

The diagnosis of Conn's syndrome in this patient was easy because of the prompt initial measurement of electrolytes by the general practitioner. The figure shows how the subsequent rise in plasma K^+ , due first probably to spontaneous variation in tumour secretion of aldosterone, and then to suppression of Ca^{++} -dependent secretion, caused the typical changes to be diminished and then masked altogether. During further research, we found that 1049 out of 6211 treated hypertensives (17%) now receive a Ca^{++} -blocker. Definitive conclusions from one case are unwise, and a formal prevalence study of Conn's syndrome in primary care seems overdue. Meanwhile we reiterate the importance of plasma electrolyte measurement before starting therapy, and recommend consideration of the diagnosis in any patient with plasma Na^+ and K^+ in the upper and lower parts of their range, respectively, prior to Ca^{++} -channel blockade.

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