CASE REPORT

Double hit! A unique case of resistant hypertension

Kristen Elizabeth DeCarlo,¹ Nidhi Agrawal²

¹Division of General Internal Medicine and Geriatrics, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

²Division of Endocrinology, Diabetes, and Metabolism, Department of Medicine, NYU School of Medicine, New York City, New York, USA

Correspondence to

Dr Kristen Elizabeth DeCarlo, kristen.decarlo@northwestern.edu and Dr Nidhi Agrawal, Nidhi.Agrawal@nyumc.org

Accepted 7 December 2017

SUMMARY

A middle-aged woman with obesity, hyperlipidaemia and diet-controlled diabetes was referred for resistant hypertension. Her blood pressure (BP) was uncontrolled on five medications, including a diuretic. Physical exam revealed a systolic ejection murmur, and ECHO demonstrated moderate hypertrophy. Laboratory examination revealed elevated aldosterone level (20.7 ng/dL) and elevated aldosterone:renin ratio (41.4 (ng/dL)/(ng/mL/h)), meeting criteria for primary aldosteronism (PA), and confirmed by saline infusion testing. CT scan of the adrenals was non-localising. Adrenal venous sampling confirmed bilateral idiopathic adrenal hyperplasia. Concurrent primary hyperparathyroidism was demonstrated by elevated calcium and parathyroid hormone levels and localised by sestamibi scan. Idiopathic adrenal hyperplasia was treated medically with spironolactone. Her BP remained elevated until postparathyroidectomy. Evidence shows that a hyperfunctioning parathyroid gland may contribute to maintaining hyperaldosteronism in PA making this bidirectional link unique. The significance of this case is in the potential for further understanding of the pathophysiology of common causes of secondary hypertension.

BACKGROUND

Primary aldosteronism (PA) is a common cause of arterial hypertension with a prevalence of 11.2% in patients with newly diagnosed hypertension.^{1 2} PA is divided into two main subtypes: aldosterone-producing adenoma (APA) and idiopathic adrenal hyperplasia (IHA).¹ The stimulus for the inappropriate elevation of aldosterone in patients with resistant hypertension is thought to be autonomous from the renin-angiotensin system; however, the underlying mechanism of PA remains unclear. The association of PA with increased incidence of cardiovascular morbidity and mortality is well established but cannot be explained by arterial hypertension alone.³

Primary hyperparathyroidism (PPTH) is a common adult endocrine disorder with a prevalence of 1 in 500–1000 population.⁴ PPTH is characterised by the overproduction of parathyroid hormone (PTH), resulting in hypercalcaemia from an adenoma (80%–85%), hyperplasia (15%–39%) and parathyroid carcinoma (<1%).⁵ Arterial hypertension develops in 56%–80% of patients with PPTH and patients with PPTH have increased risk of death from cardiovascular disease.⁶

A bidirectional link between the adrenocortical zona glomerulosa and the parathyroid gland

whereby excess PTH in PPTH may play a role in maintaining hyperaldosteronism in PA has been described.⁷ The underlying mechanism linking excess PTH to increased blood pressure has been shown in vitro where PTH stimulates secretion of aldosterone from human adrenocortical cells in a concentration-dependent fashion.⁸ Gene expression and immunohistochemistry studies have subsequently demonstrated expression of type 1 PTH receptors in the cytoplasm of APA cells in a patient with PA and concurrent PPTH, providing evidence that PTH could influence the synthesis of aldosterone. Furthermore, the expression of mineralocorticoid receptor (MR) transcript was found in the nuclei of PTH-secreting adenoma and in normal parathyroid gland tissue.⁷ In summary, these findings provide evidence that PTH may have a role in PA via adrenocortical cell proliferation and/or aldosterone secretion.^{7–9}

We herein report the case of a patient who presented with resistant hypertension and hypercalcaemia that was found to have PA from IHA with concurrent PPTH, which subsequently resolved after parathyroid surgery.

CASE PRESENTATION

A 52-year-old woman with a history of obesity, hyperlipidaemia and diet-controlled diabetes was referred to endocrinology clinic for the evaluation of resistant hypertension (figure 1). She was diagnosed with hypertension at the age of 32 years. Work up of hypertension on initial diagnosis is not available; however, the patient denied history of easy bruisability, striae, episodic headaches, flushing, palpitations, tremors and heat or cold intolerance. She has no personal history of steroid use. On initial evaluation for resistant hypertension, she was prescribed the following regimen: hydralazine 50 mg twice daily, labetalol 300 mg twice daily, hydrochlorothiazide 25 mg daily, nifedipine 90 mg daily and spironolactone 25 mg daily. She had a family history of primary (essential) hypertension.

Physical examination

On presentation, blood pressure was 149/102 mm Hg with a heart rate of 58 bpm; the body mass index was 48.7 kg/m². Neck exam revealed an enlarged goitre and no bruits. Cardiac exam demonstrates an II/VI non-radiating, systolic ejection murmur best heard at the base of the heart. No abdominal bruits were auscultated, and no oedema was appreciated in the extremities. A transthoracic echocardiogram showed a normal systolic function (left ventricular (LV) ejection fraction 55%), moderate LV hypertrophy and severely hypokinetic

CrossMark

To cite: DeCarlo KE, Agrawal N. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-221530

Time	August 2016	October 2016	November 2016	December 2016	February 2017	April 2017
Blood Pressure (mmHg)	149/102	155/110	172/102	148/93	146/100	131/83
Medications	Hydral, HCTZ, Labet, Nifed, Spiro	Carved, Chlor, Nifed, Spiro	Carved, Nifed, ACE, AML	Carved, Nifed, ACE (↑), AML	Carved, Nifed, ACE, AML, Spiro	
Lab Tests	Ca: 12.4 mg/dL iCa: 5.5 mg/dL PTH: not available Aldo: not available Renin: 0.78 ng/mL/h	Ca: 11.2 mg/dL iCa: 5.5 mg/dL PTH: 131.2 pg/mL Aldo: not available Renin: 0.78 ng/mL/h	Ca: 11.0 mg/dL PTH: not available Aldo: 20.7 ng/dL Renin: 0.50 ng/mL/h			Ca: 9.7 mg/dL PTH: 49.5 pg/mL
Diagnoses & Interventions	Resistant Hypertension	Suspect PA Suspect PPTH	DXA normal Renal US normal Sestamibi localized Diagnosis of PPTH	CT abdomen normal Diagnosis of PA (Saline infusion)	AVS Lat index: 1.3 Diagnosis of IAH	Ptx (Adenoma)

Figure 1 Time course of the clinical case. Normal ranges: aldosterone (aldo)=3–15 g/dL; calcium (Ca)=8.0–10.4 mg/dL; ionised calcium (iCa)=4.6–5.2 mg/dL; parathyroid hormone (PTH)=14–72 pg/mL; plasma renin=0.65–5.0 ng/mL/h. Upward arrow indicates increased medication dose. ACE, lisinopril; AML, amlodipine; Carved, carvedilol; Chlor, chlorthalidone; HCTZ, hydrochlorothiazide; Hydral, hydralazine; IAH, idiopathic adrenal hyperplasia; Labet, labetalol; Lat index, lateralis ation index; Nifed, nifedipine; PA, primary aldosteronism; PPTH, primary hyperparathyroidism; Ptx, parathyroidectomy; Renin, plasma renin; Spiro, spironolactone.

basal inferoseptum. A nuclear stress test demonstrated no significant evidence of stress-induced ischaemia. Her clinic blood pressure measurements remained elevated with systolic pressure between 145 mm Hg and 200 mm Hg, and her diastolic blood pressure was between 95 mm Hg and 135 mm Hg.

INVESTIGATIONS

Laboratory values and imaging tests

Spironolactone and thiazide diuretics were held from the treatment regimen for 5 weeks prior to serum testing to avoid alterations in aldosterone and plasma renin levels and the induction of mild hyperparathyroidism, respectively. Lisinopril 20 mg and amlodipine 10 mg were initiated. Plasma aldosterone was 20.7 ng/dL (normal range 3–15 g/dL), plasma renin was 0.50 ng/mL/h (normal range 0.65–5.0 ng/mL/h) and aldosterone:renin ratio (ARR) was 41.4 (ng/dL)/(ng/mL/h), thereby meeting criteria for PA. Saline infusion test was confirmatory for hyperaldosteronism with a plasma aldosterone concentration of 19.4 ng/dL and plasma renin of 0.41 ng/mL/h. A 24-hour urine collection demonstrated a urine calcium level of 336 mg/24 hours and a urine creatinine of 1.42 g/24 hours. A contrast abdominal and pelvis CT was unremarkable, including normal adrenal glands bilaterally (figure 2). Adrenal vein sampling (AVS) demonstrated right and left adrenal vein selectivity index of 42.6 and 9.2, respectively, with a lateralisation index was 1.3, confirming symmetric production of aldosterone from the bilateral adrenal glands and the diagnosis of IHA. Work ups for Cushing's disease and pheochromocytoma were negative.

The patient was normokalaemic (3.7–4.4 mEq/L), total calcium (Ca) was 11.2 mg/dL (normal Ca range 8.0–10.4 mg/dL, ionised calcium (iCa) was 5.5 mg/dL (normal iCa range 4.6–5.2 mg/dL), albumin 4.2 g/dL, corrected Ca was 11.0 mg/dL, and plasma creatinine was 1.4 mg/dL (Glomerular Filtration Rate (GFR) 47 mL/min/1.73 m²). Intact parathyroid hormone (iPTH) was 131.2 pg/mL (normal range 14–72 pg/mL), serum phosphorus was 2.4 mg/dL and 25-hydroxyvitamin D was 30.8 ng/mL suggesting PPTH.

Figure 2 Non-contrast CT abdomen and pelvis. The liver, spleen, and pancreas are unremarkable. Normal appearance of the bilateral adrenal glands at the level of the suprarenal fossa. There is no evidence of adrenal mass or cyst. Arrow identifies location of the adrenal gland.

Neck ultrasound with Doppler showed an enlarged and nodular thyroid gland with a hypoechoic 0.9×0.8×0.8 cm delineated lesion in the inferior left lobe with scant flow, likely correlating to a parathyroid adenoma. A technetium sestamibi scan showed a focal area of persistent uptake in the left lower thyroid. Dual-energy x-ray absorptiometry (DXA) scan was normal, and an abdominal ultrasound was negative for kidney stones.

OUTCOME AND FOLLOW-UP

Hyperaldosteronism from IHA was treated medically with an aldosterone antagonist with blood pressure regimen including spironolactone 25 mg daily, lisinopril 40 mg daily, nifedipine 90 mg daily and chlorthalidone 25 mg daily. Her clinic blood pressure measurements remained elevated with systolic pressure between 138 mm Hg and 172 mm Hg, and her diastolic blood pressure was between 92 mm Hg and 100 mm Hg.

The patient subsequently underwent an uncomplicated left inferior parathyroid adenoma removal. Intraoperative PTH monitoring demonstrated a sharp downward trend (initial PTH level was 288 pg/mL and decreased to 110 pg/mL, subsequently 42 pg/mL to 30 pg/mL and finally 26.7 pg/mL), indicating a successful parathyroidectomy was performed. Histology showed enlarged hypercellular parathyroid gland consistent with adenoma. Postoperative iPTH and calcium normalised (49.5 pg/mL and 9.7 mg/dL, respectively) and 25-hydroxyvitamin D was 22.8 ng/mL. The patient received aggressive vitamin D repletion with ergocalciferol 50 000 units weekly. Postoperative blood pressure measurements improved with systolic pressure between 123 mm Hg and 138 mm Hg, and her diastolic blood pressure was between 75 and 86 mm Hg. Optimal blood pressure control has been maintained postoperatively with lisinopril 40 mg and spironolactone 25 mg only.

DISCUSSION

Hypertension is a risk factor of cardiovascular disease and affects up to one in three adults in the USA with a prevalence of 30.9% in patients over 18 years.¹⁰ A minority of these patients meets diagnostic criteria for secondary hypertension with a clear aetiology underlying increased blood pressure. PA is among the most

common cause of secondary hypertension, and cases of hypertensive patients with PA and concurrent PPTH are emerging in the literature. A retrospective report from a centre for secondary hypertension in Rome found 2.6% of patients treated for PA over a 9-year period had concurrent PPTH (8 out of 306 patients).¹¹ The significance of these cases lies in the potential for further understanding of the pathophysiology of common causes of resistant hypertension and may help lead to eventually discover the link between PA, PPTH and cardiovascular disease.^{8 12} In an effort to report these unique cases, a registry has been established to foster further research.⁸

Hyperparathyroidism has long been described as an independent risk factor of cardiovascular disease morbidity and mortality.^{6 12} In addition, observational studies demonstrate elevated PTH in association with higher risk of hypertension, LV hypertrophy, arrhythmia, diabetes and hyperlipidaemia.^{13–15} In a study of patients with PA due to APA, there was a 31% increase in serum PTH as compared with patients with comparable primary (essential) hypertension, demonstrating that elevated PTH is a feature in some patients with PA.⁹ This observation is significant in the context of an emerging body of evidence suggesting that a hyperfunctioning parathyroid gland may contribute to maintaining hyperaldosteronism in PA. The basis of this interplay is related to several observations including in vitro studies showing that PTH increased aldosterone secretion from adrenocortical cells in a concentration-dependent manner.^{7 8} Gene expression and immunohistochemistry studies show PTH receptors in APAs and MR receptors in parathyroid cells. The significance of experimental studies demonstrating the expression of the PTH receptor in the cytoplasm of APA cells lies in the hypothesis that PTH may directly influence the synthesis of aldosterone and thus provide a pathway to describe the persistent state of hyperaldosteronism and hypertension in similar cases.⁸ The mechanism driving persistent hyperaldosteronism is an area of uncertainty. In the setting of normal or high levels of NaCl, aldosterone secretion is stimulated, causing sodium and water retention, thereby resulting in arterial hypertension and suppression of the renin–angiotensin system. This cascade is expected to blunt the secretion of aldosterone; however, as seen in this case, persistent aldosterone secretion is observed in spite of an expected suppression of the renin–angiotensin system. Excess PTH leading to persistent aldosterone secretion provides a possible explanation. This is supported by the observation in this case that parathyroidectomy (removal of PTH-secreting adenoma) resulted in a fall in blood pressure, which was not observed with medical therapy alone.^{8 9} While this association could be purely coincidental, collectively, these results may suggest the existence and clinical significance of a bidirectional relationship between the adrenocortical zona glomerulosa and the parathyroid gland.^{8 9}

A ‘calcium paradox’ provides an explanation for the relationship between PA and excess PTH. A study of aldosterone infusion in rats subjected to a 1% NaCl treatment demonstrated enhanced urinary calcium and magnesium excretion, subsequent lowered ionised extracellular serum calcium levels and elevated PTH levels.¹⁶ Of consequence, in spite of urinary calcium losses, total intracellular and cytosolic free calcium concentrations are increased in the hyperaldosteronism state, thus a ‘calcium paradox’. The oxidative and nitrosative stress induced by intracellular calcium may contribute to a proinflammatory vascular phenotype and increased cardiovascular risk found in patients with PA and resultant secondary PTH. This well-established paradox describes the relationship between PA and secondary PTH.^{16 17} This case demonstrates primary rather than secondary hyperparathyroidism, as evidenced by the elevated serum and

iCa levels, elevated PTH level and a left inferior parathyroid adenoma. Furthermore, intraoperative PTH levels decreased precipitously (from 288 pg/mL to 26.7 pg/mL) in the setting of parathyroid adenoma removal, providing additional support that this case demonstrates concomitant hyperaldosteronism from IHA and PPTH.

Several questions arise in regards to this case presentation. Screening for PA is indicated in the setting of resistant hypertension, unprovoked hypokalaemia or adrenal incidentaloma.^{18 19} The evaluation of PA in this case is on the basis of resistant hypertension without evidence of hypokalaemia or adrenal incidentaloma. Of interest, in a study of hypertensive patients, hypokalaemia was observed in 48% of patients with APA and only 17% of those with IHA.⁸ It is widely accepted that hypokalaemia is not a required diagnostic criteria of PA, but the distinction between IHA from low-renin primary (essential) hypertension remains an area of debate. In this case, the saline infusion test confirms the diagnosis of PA, making a form of low-renin hypertension a less likely diagnosis.^{18 19}

PA is divided into the medically treatable IHA and the surgically treatable APA; of significance, AVS is required to differentiate these diagnoses. AVS is an invasive, costly procedure that is not widely available. An algorithm for selecting the patients who are more likely to require AVS has been proposed based on accumulating evidence that PTH may play a role in PA. A prospective study of hypertensive patients concluded that an elevated ARR (greater than 29 (ng/dL)/(ng/mL/h)) with an elevated PTH level (greater than 80 ng/L) tends to be a feature of APA, providing an algorithm for identifying patients who benefit from AVS.²⁰ In this case, the above criteria were met, AVS was performed and the lateralisation index demonstrated IHA rather than APA. Medical management was initiated for the treatment of IHA with low dose MR blockade. MR antagonist titration was not achieved prior to parathyroidectomy and further titration postoperatively was not required, as adequate blood pressure control has been maintained on an ACE inhibitor and low dose MR blockade.

The relationship between aldosterone and PTH is an active area of research, as the mechanisms and modulators of their interplay may have significant impact in understanding their role in cardiovascular disease. A prospective cohort study designed to evaluate the relationship between plasma aldosterone, ARR and PTH found that aldosterone and ARR are independent predictors of higher PTH concentrations. Furthermore, aldosterone and PTH were independently associated with cardiovascular death in patients with aldosterone and PTH concentrations above the median.²¹ Given the identification of cardiovascular risk by both of these hormones, studies have been developed to evaluate whether MR antagonism impacts PTH secretion and CV health. In one such study, patients with PPTH treated with eplerenone demonstrated no significant effect on circulating PTH levels. This study has several limitations, including a single-centre design, small sample size and short treatment period. Furthermore, this study may not be directly generalisable to patients with hyperaldosteronism.²² The treatment period is of particular interest, as in vivo studies of patients without PA or PPTH have shown that angiotensin II infusion acutely stimulates PTH secretion and administration of ACE inhibitors acutely lowers PTH secretion; however, infusion of aldosterone results in unchanged PTH levels in the short term. This observation implies that angiotensin II may be the acute stimulus of PTH secretion. In the same study, chronic MR antagonism showed modestly lower PTH levels, whereas the placebo group had a slight decrease in serum calcium and mild increase in PTH compared with the treatment group. These findings suggest that chronic MR

antagonism has a PTH blunting effect and that aldosterone may be involved in the modulation of PTH in the chronic setting.²³ In this case, we speculate that chronically elevated PTH influenced aldosterone synthesis, and future studies in patients with PA or PPTH will be critical in uncovering the pleiotropic relationships between aldosterone and PTH.

In this case presentation, a patient referred for the evaluation of resistant hypertension was found to have PA secondary to IHA. Concurrently, the patient was diagnosed with PPTH from a parathyroid adenoma. Of significance, normalisation of blood pressure was not achieved with medical management of IHA alone; rather normotension was observed only after surgical removal of the parathyroid adenoma and normalisation of PTH. This case exemplifies the bidirectional relationship previously described, whereby treatment of PA with MR antagonist alone was not sufficient to suppress hyperaldosteronism prior to surgical removal of the PTH secreting parathyroid adenoma. In summary, this case demonstrates a unique clinical scenario that may aid in the elucidation of the physiological interplay between the adrenocortical zona glomerulosa in PA and the hyperparathyroid state. Further evaluation of the pathophysiology leading to PA and prevention of persistent resistant hypertension will be important for the basis of future research in this field. The functional link between aldosterone and PTH may represent an additional pathway of renin–angiotensin–aldosterone mediated organ damage, and future evidence will need to be established to identify the significance of these pathways and their relationship in mediation of arterial hypertension and risk of cardiovascular disease.²⁴

Learning points

- Primary aldosteronism and primary hyperparathyroidism are both independently associated with an increased incidence of cardiovascular morbidity and mortality.
- A subset of patients diagnosed with secondary hypertension from primary aldosteronism has been found to have concomitant hyperparathyroidism.
- Evidence suggests that the parathyroid gland may contribute to maintaining hyperaldosteronism in primary hyperaldosteronism.
- A bidirectional link between the adrenocortical zona glomerulosa and the parathyroid gland may represent a significant relationship in the underlying pathophysiology of resistant hypertension.

Acknowledgements Dr. Jennifer B. Ogilvie performed the parathyroidectomy and participated in the care of this patient.

Contributors Dr. Agrawal was the attending endocrinologist caring for the patient described in the case. Dr. DeCarlo completed chart review and background research to write and report this case in conjunction with Dr. Agrawal. The investigators retained full independence in the conduct of this research.

Funding The research reported in this case report was supported by New York University School of Medicine.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Funder JW, Carey RM, Mantero F, *et al.* The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2016;101:1889–916.
- 2 Rossi GP, Bernini G, Caliumi C, *et al.* A prospective study of the prevalence of primary aldosteronism in 1,125 hypertensive patients. *J Am Coll Cardiol* 2006;48:2293–300.
- 3 Milliez P, Girerd X, Plouin PF, *et al.* Evidence for an increased rate of cardiovascular events in patients with primary aldosteronism. *J Am Coll Cardiol* 2005;45:1243–8.
- 4 Yeh MW, Ituarte PH, Zhou HC, *et al.* Incidence and prevalence of primary hyperparathyroidism in a racially mixed population. *J Clin Endocrinol Metab* 2013;98:1122–9.
- 5 Adami S, Marcocci C, Gatti D. Epidemiology of primary hyperparathyroidism in Europe. *J Bone Miner Res* 2002;17(Suppl 2):N18–23.
- 6 Hedbäck GM, Odén AS. Cardiovascular disease, hypertension and renal function in primary hyperparathyroidism. *J Intern Med* 2002;251:476–83.
- 7 Mazzocchi G, Aragón F, Malendowicz LK, *et al.* PTH and PTH-related peptide enhance steroid secretion from human adrenocortical cells. *Am J Physiol Endocrinol Metab* 2001;280:E209–13.
- 8 Maniero C, Fassina A, Guzzardo V, *et al.* Primary hyperparathyroidism with concurrent primary aldosteronism. *Hypertension* 2011;58:341–6.
- 9 Maniero C, Fassina A, Seccia TM, *et al.* Mild hyperparathyroidism: a novel surgically correctable feature of primary aldosteronism. *J Hypertens* 2012;30:390–5.
- 10 Centers for Disease Control and Prevention (CDC). Vital signs: prevalence, treatment, and control of hypertension—United States, 1999–2002 and 2005–2008. *MMWR Morb Mortal Wkly Rep* 2011;60:103–8.
- 11 Concistré A, Petramala L, Zinamosca L, *et al.* Primary aldosteronism with concurrent primary hyperparathyroidism: clinical case load in a single centre. *Eur Rev Med Pharmacol Sci* 2015;19:971–6.
- 12 Tomaschitz A, Ritz E, Pieske B, *et al.* Aldosterone and parathyroid hormone: a precarious couple for cardiovascular disease. *Cardiovasc Res* 2012;94:10–19.
- 13 Kamycheva E, Sundsfjord J, Jorde R. Serum parathyroid hormone level is associated with body mass index. The 5th Tromsø study. *Eur J Endocrinol* 2004;151:167–72.
- 14 Nilsson IL, Aberg J, Rastad J, *et al.* Left ventricular systolic and diastolic function and exercise testing in primary hyperparathyroidism—effects of parathyroidectomy. *Surgery* 2000;128:895–902.
- 15 Morfís L, Smerdely P, Howes LG. Relationship between serum parathyroid hormone levels in the elderly and 24 h ambulatory blood pressures. *J Hypertens* 1997;15:1271–6.
- 16 Vidal A, Sun Y, Bhattacharya SK, *et al.* Calcium paradox of aldosteronism and the role of the parathyroid glands. *Am J Physiol Heart Circ Physiol* 2006;290:H286–H294.
- 17 Chhokar VS, Sun Y, Bhattacharya SK, *et al.* Hyperparathyroidism and the calcium paradox of aldosteronism. *Circulation* 2005;111:871–8.
- 18 Kaplan NM. Is there an unrecognized epidemic of primary aldosteronism? *Con. Hypertension* 2007;50:454–8.
- 19 Sahay M, Sahay RK. Low renin hypertension. *Indian J Endocrinol Metab* 2012;16:728–39.
- 20 Rossi GP, Ragazzo F, Seccia TM, *et al.* Hyperparathyroidism can be useful in the identification of primary aldosteronism due to aldosterone-producing adenoma. *Hypertension* 2012;60:431–6.
- 21 Tomaschitz A, Pilz S, Rus-Machan J, *et al.* Interrelated aldosterone and parathyroid hormone mutually modify cardiovascular mortality risk. *Int J Cardiol* 2015;184:710–6.
- 22 Tomaschitz A, Verheyen N, Meintzer A, *et al.* Effect of eplerenone on parathyroid hormone levels in patients with primary hyperparathyroidism: results from the EPATH randomized, placebo-controlled trial. *J Hypertens* 2016;34:1347–56.
- 23 Brown JM, Williams JS, Luther JM, *et al.* Human interventions to characterize novel relationships between the renin–angiotensin–aldosterone system and parathyroid hormone. *Hypertension* 2014;63:273–80.
- 24 Pilz S, Kienreich K, Drechsler C, *et al.* Hyperparathyroidism in patients with primary aldosteronism: cross-sectional and interventional data from the GECOH study. *J Clin Endocrinol Metab* 2012;97:E75–9.

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow