

## CASE REPORT

# Hyperprolactinaemia in a patient with kidney failure

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## ABSTRACT

Hyperprolactinaemia is a common endocrine abnormality in patients with kidney failure. A 43-year-old female, known with kidney failure on maintenance haemodialysis, was referred with symptomatic hyperprolactinaemia. Biochemical investigations revealed a markedly elevated serum prolactin level. Magnetic resonance imaging of the brain (without gadolinium) demonstrated a pituitary macroadenoma. The patient was started on cabergoline therapy. This case discusses hyperprolactinaemia in kidney failure and highlights the importance of investigating markedly elevated prolactin levels. In cases where patients have galactorrhoea, headaches and/or visual disturbances, clinicians should be alert to the possibility of a prolactin-secreting pituitary tumour.

**Keywords:** hyperprolactinaemia; prolactinoma; kidney failure.

## INTRODUCTION

Hyperprolactinaemia is a common biochemical finding associated with pituitary tumours, medication, pituitary stalk disorders, pregnancy, primary hypothyroidism, chest-wall lesions (in the T4 dermatome) and kidney failure [1]. They are the commonest hormone-secreting pituitary tumour in adults [2].

Macroprolactinomas measure more than 10 mm in diameter, whereas microprolactinomas are less than 10 mm [3]. The clinical manifestations of hyperprolactinaemia vary depending on the patient's age and sex. Females typically present with galactorrhoea and oligo/amenorrhoea whereas men complain of erectile dysfunction and loss of libido [4]. Symptoms of mass effect, such as headaches, visual field disturbances and cranial neuropathies, may also be observed [2]. Serum prolactin levels correlate with the aetiology; a prolactin level greater than 250 µg/L is indicative of a prolactinoma whereas a level of more than 500 µg/L is diagnostic of a macroprolactinoma [3].

Hyperprolactinaemia is a common endocrine abnormality in patients with kidney failure [4,5]. In patients with hyperprolactinaemia who present with headaches and visual abnormalities, a high index of suspicion should be maintained for a prolactinoma. This case report highlights

that patients with extremely high prolactin levels, despite kidney failure, need to be investigated for a prolactinoma.

## CASE DESCRIPTION

A 43-year-old female was referred to the endocrine department for workup of hyperprolactinaemia. She reported secondary amenorrhoea for two years, recent onset of headaches, visual disturbances and bilateral galactorrhoea.

Regarding her past medical history, she had kidney failure secondary to hypertension and had been treated with chronic haemodialysis (thrice-weekly sessions of 4 hours each) since 2018. She had human immunodeficiency virus infection, which was virologically suppressed on abacavir, lamivudine and efavirenz. Her other chronic medications included hydralazine, furosemide, atenolol, doxazosin, amlodipine and one-alpha vitamin D. She was not pregnant.

Examination revealed spontaneous galactorrhoea. The neurological examination was normal, with no bitemporal hemianopia. The rest of the clinical examination was unremarkable. Biochemical investigations revealed a prolactin level of 603.7 µg/L (normal range 4.8–23.3 µg/L).

The rest of her biochemical workup, including previous elevated prolactin levels, are shown in Table 1.

Based on the elevated prolactin levels, which were out of keeping with kidney failure, magnetic resonance imaging (MRI) of the brain was performed. Gadolinium-based contrast was not used, to avoid the risk of nephrogenic systemic fibrosis. The MRI showed a sellar mass, measuring 15 mm transverse × 10 mm anteroposterior × 7 mm craniocaudal (Figure 1). A diagnosis of a prolactin-secreting pituitary adenoma (macroprolactinoma) was made and the patient was started on cabergoline therapy.

## DISCUSSION

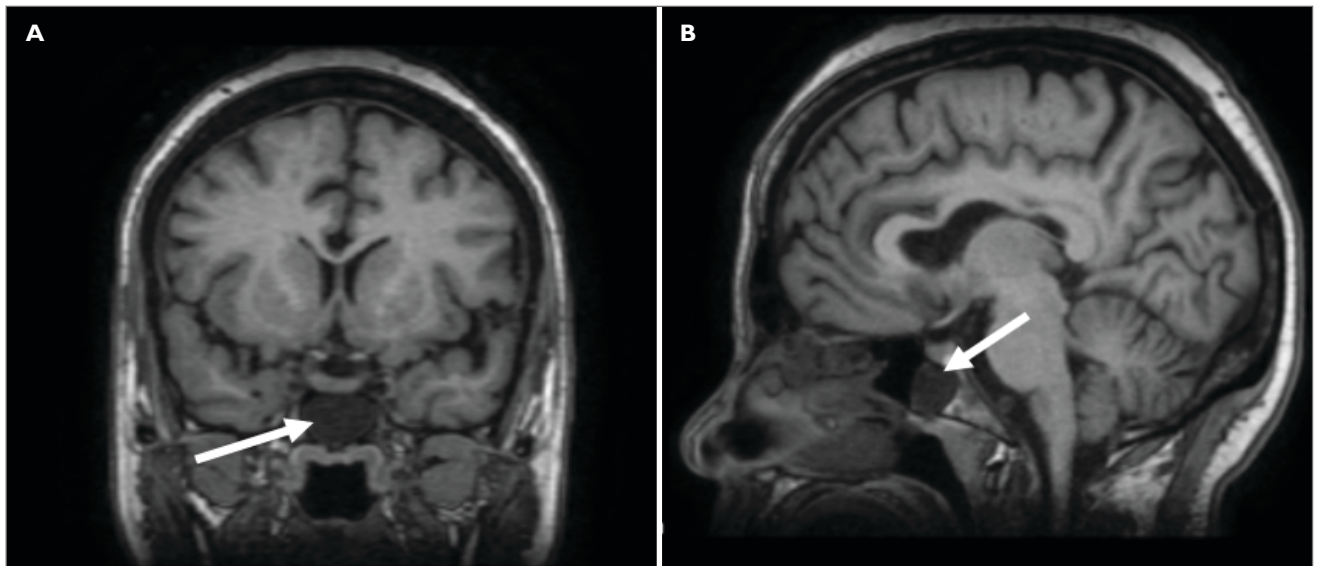
The prevalence of hyperprolactinaemia in patients with kidney failure ranges between 52–81% [5–8]. Hyperprolactinaemia is found in patients undergoing both haemodialysis and peritoneal dialysis [7]. Higher serum prolactin levels are described in females [8,9]. However, there is no clear association between serum prolactin level and patient age, the type of dialysis or the frequency of dialysis [8]. Prolactin levels increase as kidney function decreases, with the highest prolactin levels seen in patients with kidney failure on regular haemodialysis [10]. There is no difference in prolactin levels pre- and post-haemodialysis [11], or with thrice-weekly versus six-times per week dialysis [8]. The mean serum prolactin in patients on both haemodialysis and peritoneal dialysis ranges from 33.2–65.2 µg/L [5,7,8]. The maximum prolactin levels in patients on haemodialysis ranges between 126.6–346.5 µg/L [5,7,10].

The precise pathophysiology causing hyperprolactinaemia in kidney failure is unknown but is likely multifactorial. The first mechanism is related to reduced glomerular filtration rate (GFR), as prolactin clearance is reduced by 33% in kidney failure [12] and prolactin levels are shown to normalise six months post kidney transplant [13]. Additional mechanisms are independent of GFR. There is alteration of dopaminergic pathways, evidenced by resistance of dopamine to both stimulation and suppression [5,9,12,14]. This has been attributed to dopamine receptor downregulation [12], illustrated by a blunted response of prolactin to thyrotropin-releasing hormone [9] and failure to suppress prolactin with a single dose of bromocriptine [9] or dopamine infusion [12]. However, a six-week course of bromocriptine has been shown to suppress prolactin [9]. In patients with kidney failure, the circadian rhythm of prolactin disappears, and they have diminished physiological oscillations of prolactin secretion, leading to a longer half-life of prolactin. This, coupled with a lower clearance rate, results in elevated prolactin levels [15]. Other postulated mechanisms include total body zinc depletion and secondary hyperparathyroidism [14].

In patients with kidney failure who present with hyperprolactinaemia, drugs need to be excluded as a cause. Drugs commonly used in kidney failure that may cause hyperprolactinaemia include anti-hypertensives (verapamil and  $\alpha$ -methyldopa), antidepressants, metoclopramide and antihistamines [1,3,9].

**Table 1.** Biochemical investigations in a patient with a macroprolactinoma.

	2 years before presentation	1 year before presentation	At current presentation	Reference range
Urea (mmol/L)			25.1	2.1–7.1
Creatinine (µmol/L)			632	49–90
Estimated glomerular filtration rate (mL/min/1.73 m <sup>2</sup> )			6	>89
Prolactin (µg/L)	293.8	287.6	603.7	4.8–23.3
Monomeric prolactin (µg/L)			432.4	3.5–18
Parathyroid hormone (pmol/L)			86.1	1.6–6.0
Thyroid stimulating hormone (mIU/L)			1.53	0.35–5.5
Thyroxine (pmol/L)			18.1	11.5–22.7
Adrenocorticotrophic hormone (pmol/L)			2.8	1.6–13.9
Follicle stimulating hormone (IU/L)			4.5	
Luteinising hormone (IU/L)			0.7	
Oestradiol (pmol/L)			<19	
Human growth hormone (µg/L)			0.9	
Insulin-like growth factor (µg/L)			115	58–219



**Figure 1.** Magnetic resonance imaging (without gadolinium) of the brain, showing a pituitary macroadenoma measuring 15 mm transverse x 10 mm anteroposterior x 7 mm craniocaudal (arrows), without any compression of the optic chiasm and no cavernous sinus encasement. A, coronal and B, sagittal T1 weighted images.

Once drug causes have been excluded, an MRI scan is necessary to exclude a prolactinoma. The Endocrine Society guidelines recommend medical treatment with a dopamine agonist as first-line therapy for all prolactinomas [3]. Both cabergoline and bromocriptine may be used in patients with kidney failure [4,6]. Cabergoline and bromocriptine are renally excreted in the order of 20% and 6%, respectively, and hence require no dose adjustment. Cabergoline is recommended, as it has greater efficacy in normalising prolactin levels and shrinkage of tumour size [3].

## CONCLUSIONS AND LEARNING POINTS

A significant proportion of patients with kidney failure have hyperprolactinaemia, usually less than 100 µg/L. If patients are symptomatic or have markedly elevated levels of prolactin (>200 µg/L), this should direct the clinician to investigate further; levels >500 µg/L are diagnostic of a macroadenoma. Associated galactorrhoea, headaches or visual disturbances should alert the clinician to the presence of a possible prolactinoma. MRI of the pituitary fossa is the gold standard imaging modality for diagnosing pituitary adenomas.

## Ethical considerations

Ethical clearance was granted by the University of the Witwatersrand's Human Research Ethics Committee – protocol number M200776.

## REFERENCES

1. Majumdar A, Mangal NS. Hyperprolactinaemia. *J Hum Reprod Sci.* 2013; 6(3):168-175.
2. Vroonen L, Daly AF, Beckers A. Epidemiology and management challenges in prolactinomas. *Neuroendocrinology.* 2019; 109:20-27.
3. Melmed S, Casanueva FF, Hoffman AR, Kleinberg DL, Montori VM, Schlechte JA, et al. Diagnosis and treatment of hyperprolactinaemia: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2011; 96(2):273-288.
4. Meuwese CL, Carrero JJ. Chronic kidney disease and hypothalamic pituitary axis dysfunction: the chicken or the egg? *Med Res Arch.* 2013; 44:591-600.
5. Nehru D, Kandasamy S, Chandramouli RK, Muthumani L. Evaluation of serum prolactin level in chronic kidney disease. *Asian J Pharm Clin Res.* 2016; 9(4):201-203.
6. Husain SI. Serum prolactin level and inflammation in chronic kidney disease. *Int J Med Health Res.* 2017; 3(2):187-189.
7. Yavuz D, Topçu G, Özener C, Akalin S, Sirikçi O. Macroprolactin does not contribute to elevated levels of prolactin in patients on renal replacement therapy. *Clin Endocrinol.* 2005; 63:520-524.
8. Lo JC, Beck GJ, Kaysen GA, Chan CT, Kliger AS, Rocco MV, et al. Hyperprolactinaemia in end-stage renal disease and effects of frequent hemodialysis. *Hemodialysis Int.* 2017; 21:190-196.
9. Gomez F, De La Cueva R, Wauters J-P, Lemarchand-Beraud T. Endocrine abnormalities in patients undergoing long-term hemodialysis: the role of prolactin. *Am J Med.* 1980; 68:522-530.
10. Cowden E A, Ratcliffe WA, Ratcliffe JG, Dobbie JW, Kennedy AC. Hyperprolactinaemia in renal disease. *Clin Endocrinol.* 1978; 9:241-248.
11. Osman NM, Ismail AM. The Impact of hemodialysis on serum prolactin and testosterone level in CKD male patients. *J Dent Med Sci.* 2016; 15(1):61-65.
12. Sievertsen GD, Lim VS, Nakawatase C, Frohman LA. Metabolic clearance and secretion rates of human prolactin in normal subjects and in patients with chronic renal failure. *J Clin Endocrinol Metab.* 1980; 50(5):846-852.
13. Sahaa MT, Sahaa HHT, Niskanenc LK, Salmelad KT, Pasternacka AI. Time course of serum prolactin and sex hormones following successful renal transplantation. *Nephron.* 2002; 92:735-737.
14. Palmer BF. Sexual dysfunction in uremia. *J Am Soc Nephrol.* 1999; 10:1381-1388.
15. Biasoli S, Mazzali A, Foroni R, D'Andrea G, Feriani M, Chiaramonte S, et al. Chronobiological variations of prolactin in chronic renal failure. *Clin Nephrol.* 1988; 30(2):86-92.
16. Dotto PD, Bonuccelli U. Clinical pharmacokinetics of cabergoline. *Clin Pharmacokinet.* 2003; 42(7):633-645.