West Hertfordshire Hospitals NHS Trust

Therapeutic Role of Dopamine Agonists in ESRF induced Hyperprolactinemia

Case reports and Literature review

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Introduction

Moderate hyperprolactinaemia (<1000mu/l) is a common abnormal biochemical finding in patients with end-stage renal failure (ESRF). About 30% of patients with chronic renal failure and up to 80% of patients on hemodialysis have elevated prolactin levels. This is probably secondary to decreased clearance and increased production of prolactin as a result of disordered hypothalamic regulation of prolactin secretion. Correction of renal failure by transplantation may result in normoprolactinemia.

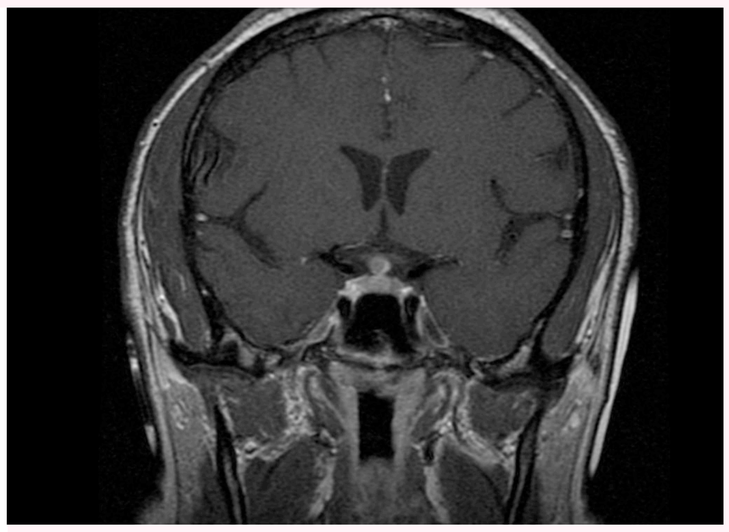
Abstract

We describe two cases whereby dopamine-agonist treatment induced regression of prolactin-related signs and symptoms in ESRF. What makes these cases unique is the fact that both patients were also found to have structural abnormalities of pituitary gland.

Case 1. A 53 year old man on haemodialysis for ESRF secondary to resistant hypertension complained of reduced libido, erectile dysfunction and painful bilateral gynaecomastia. Investigations showed a low testosterone level of 6.3nmol/l with an elevated prolactin level of 2683mu/l which was initially thought to be secondary to ESRF. Subsequent MRI of his pituitary (IMG. A) due to persisting symptoms showed a thickened pituitary stalk. He was commenced on Bromocriptine which normalised his prolactin and he improved symptomatically. Serum testosterone however remained low.

Case 2. A 69 year old man with a history of ESRF due to Focal Segmental Glomerulosclerosis on haemodialysis presented with bilateral gynaecomastia to the endocrine clinic. Investigations revealed a grossly elevated serum prolactin of 19573mu/l and a low serum testosterone of 3.0nmol/l. CT scan of pituitary (IMG. B:patient had permanent pacemaker in situ) showed a bulky pituitary fossa but no obvious macroadenoma. He was commenced on Cabergoline following which his prolactin promptly normalised with subsequent resolution of his breast symptoms. CT pituitary findings remained unchanged however.

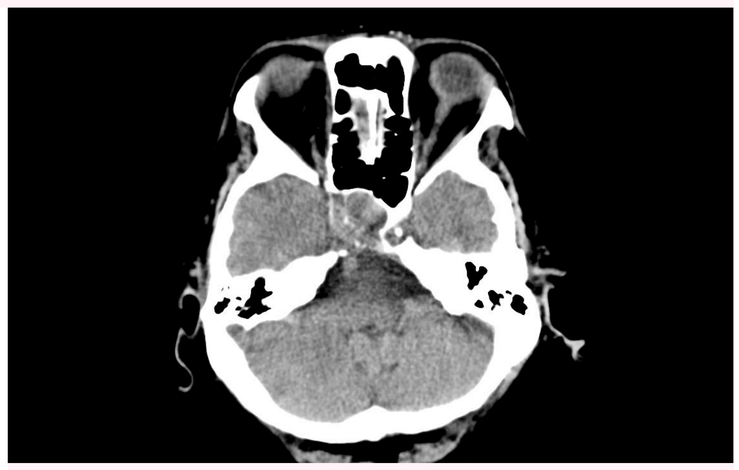
Careful review of their medications were carried out and none of them could be accountable for the raised prolactin levels.



IMG. A showing thickening of pituitary stalk

Literature review

- Prolactin response to suppressive and stimulatory agents in chronic renal failure and renal transplant patients was first reported in 1978. This case control study showed a lack of prolactin responsiveness to suppressive as well as stimulatory agents suggesting a primary pituitary disorder involving either receptor binding or postreceptor phenomena. However they could not exclude the presence of a concomitant defect either in the hypothalamus or elsewhere in the central nervous system. These disturbances seemed to be reversible, as renal transplantation not only corrected the hyperprolactinemia but also restored the responsiveness of the lactotropes to both suppressive and stimulatory agents.
- Another study looked into metabolic clearance and secretion rates of human prolactin in patient with chronic renal failure and compared it with normal subjects. The results indicated that the hyperprolactinemia associated with CRF may be due, in part, to decreased prolactin MCR(Metabolic Clearance Rate) but is primarily caused by an increase in prolactin secretion. There was a lack of response to dopamine infusion in CRF patients which suggested a lactotroph resistance to dopamine which may be a significant factor in the etiology of hyperprolactinemia associated with this disease.
- Studies on effect of long term dialysis therapy on serum prolactin in patients with chronic renal failure demonstrated a gradual decrease in hyperprolactinemia with the duration of dialysis therapy. Prolactinemia baseline values in patients dialysed for 100 months did not differ from those determined in healthy individuals.



IMG. B showing scalloping enlargement of pituitary fossa and heterogenous appearance of the gland

Conclusion

These cases illustrate that dopamine agonists clearly have a therapeutic benefit in ESRF-induced hyperprolactinaemic breast symptoms and should be considered as a potential useful medical therapy target. They do not however seem to improve hypogonadism showing that anterior pituitary dysfunction persists in some patients with chronic renal failure despite maintenance dialysis therapy.This would suggest a different mechanism affecting disturbance of the neuroendocrine hypogonadal system by ESRF.

Discussion

Unlike previous reported studies, the clinical observations notes in our cases suggest that some patients with ESRF- induced hyperprolactinemia do in fact respond to dopamine-agonist therapy thereby indicating a potentially reversible endocrine disturbance affecting the hypothalamic-pituitary dopaminergic pathways. This would also explain the normalisation of prolactin levels following renal transplantation. Possible mechanisms for this include a diminished receptor sensitivity in dopamine agonist non responders or an upregulation of the inhibitory pathway induced by the uremic process per se in susceptible patients as this endocrine phenomenon is not universally seen in all ESRF patients. The anatomical changes noted in our cases also reveal that there seems to be a stimulatory effect on lactotropic tissue which appears to be irreversible following pharmacological dopamine agonist- induced normoprolactinemia. What is unclear is whether these patients had a pre existing pituitary pathology which got exacerbated by the uremic process.

References

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