CASE REPORT

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A Complex Case of Renal Tertiary Hyperparathyroidism with a very Rare Brown Tumour of the Jaw Requiring Treatment with Initial Subtotal Parathyroidectomy followed by Maxillary Surgery and Haemodialysis

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Abstract

We describe here the case of a middle-aged woman who presented to the endocrine clinic in 2020 with chronic renal impairment and raised PTH (parathyroid hormone). The patient had seen an endocrinologist with anorexia nervosa and electrolyte abnormalities several years ago, a few times and was subsequently lost to follow-up. On this occasion her serum calcium was varying from normal to high, phosphate was normal, alkaline phosphatase high and PTH was high as well. Ultrasound of the neck suggested a radiologically U3 (indeterminate) nodule on the right lobe of thyroid and a possible parathyroid adenoma on the left which was not confirmed on sestamibi scan. The FNA (Fine needle Aspiration) of the right thyroid nodule suggested Papillary carcinoma. The patient also was found to have a Brown tumour of the maxilla, a very rare bone lesion secondary to renal hyper-parathyroidism. The patient initially underwent right haemithyroidectomy and subtotal parathyroidectomy with eventual completion left thyroidectomy. There was no improvement of this bone lesion despite lowering of PTH following subtotal parathyroidectomy and as such the patient required maxillary surgery one year later. The patiently remains currently on haemodialysis.

Key words: Renal, hyperparathyroidism, parathyroidectomy, Brown tumour, papillary carcinoma

Introduction

Tertiary hyperparathyroidism occurs when an excess of PTH is secreted by the parathyroid glands, after longstanding secondary hyperparathyroidism[1]. In secondary hyperparathyroidism (in chronic renal impairment or vitamin D deficiency), serum calcium is low or low-normal, phosphate is high, and PTH is high; and in tertiary hyperparathyroidism serum calcium, phosphate, and PTH are all raised. However, in renal hyperparathyroidism, the phosphaturia effect of PTH and FGF-23 (Fibroblast Growth Factor-23) sometimes may account for the serum phosphate level to remain normal[2]. In tertiary hyperparathyroidism, secondarily hyperplastic parathyroid glands of renal failure are no longer under secretory control of PTH by calcium, and therefore secrete more PTH and cause hypercalcaemia. The initial medical treatment with calcimimetics like Cinacalcet, vitamin D supplementation and low phosphate diet with phosphate binders, like calcium acetate or sevelamer (if serum phosphate is high) may not always be effective and the patient may require surgery in the form of subtotal parathyroidectomy or total parathyroidectomy with auto-transplantation[1]. Common indications for surgery for hyperparathyroidism in renal impairment include elevated levels of PTH, hypercalcaemia, very high phosphate (> 1.95 mmol/L), bone disease (osteitis fibrosa cystica), severe symptoms (pruritus, bone pain), and progressive ectopic calcification, and calciphylaxis[3]. Parathyroidectomy is shown to improve symptoms, bone and mineral metabolism, cardiovascular risk factors, and overall quality of life[4,5].

Case report

A 49-year-old woman was referred with chronic renal impairment and high PTH to the endocrine clinic in November 2020. She had a background history of anorexia nervosa (first seen by an endocrinologist in December 2009 with electrolyte abnormalities), osteoporosis, and had a left jaw swelling. The patient was under the care of the nephrology department at a tertiary hospital. Her medications at this point included Magnesium Oxide, Multivitamins, Alfacalcidol 1 mcg twice a week, Slow sodium tablets, Ferrous Fumarate, and Thiamine.

Her latest blood results showed serum urea 10.4 mmol/L (N: 2.5 - 7.8), creatinine 221 umol/L (N: 44 - 97), eGFR 21 mL/min, PTH 52.7 pmol/L (Normal: 2.0 - 9.3), adjusted calcium 2.50 mmol/L (N: 2.20 - 2.60), alkaline phosphatase 172 U/L (N: 30 - 130), phosphate 1.05 mmol/L (N: 0.8 - 1.45) vitamin D 50.4 nmol/L (N: 50 - 125) and Hb 111. The

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diagnosis was renal tertiary hyperparathyroidism, the serum calcium was varying from normal to elevated levels. Her serum adjusted calcium was raised at 2.70 mmol/L, 2.79 mmol/L and 2.83 mmol/L a few months ago. Her serum phosphate remained normal, and her alkaline phosphatase was persistently raised from renal osteodystrophy.

The patient's ultrasound neck showed a hypoechoic lesion adjacent to the inferior pole of the left thyroid with increasing vascularity likely to be parathyroid adenoma and a well-defined heterogeneous predominantly hypoechoic nodule in the upper pole of right lobe of thyroid with internal calcifications with predominantly peripheral vascularity, thought to be radiologically U3 (indeterminate) in nature. The patient next underwent a sestamibi scan which however showed no parathyroid adenoma.

Her FNA of the right thyroid nodule performed by the ENT Consultant suggested histologically papillary carcinoma of thyroid. The decision following a multidisciplinary team meeting, was taken to consider a subtotal parathyroidectomy, given the diagnosis of renal hyperparathyroidism, together with right hemithyroidectomy. Histological study suggested parathyroid hyperplasia and papillary carcinoma with a lymph node metastasis and the patient thereafter needed complete left thyroidectomy.

The patient subsequently was managed on Levothyroxine and Calcichew D3, together with Alfacalcidol, which were later discontinued as her serum calcium was raised (elevated at 2.98 mmol/L). Her PTH continued to remain low, between 0.5 pmol/L to 2.0 pmol/L with the latest level being 1.2 pmol/L (hypoparathyroidism).

Her biopsy of the left maxillary swelling suggested Giant cell rich lesion (Brown tumour). Brown tumour is very rare in renal hyperparathyroidism and can sometimes regress with subtotal parathyroidectomy. In this case however, the patient required partial anterior maxillectomy with obturator placement 1 year later.

The patient has now been receiving haemodialysis twice a week at a tertiary hospital as the eGFR was varying between 9 - 11 mL/min and the creatinine between 438 to 476 umol/L.

Discussion

Renal hyperparathyroidism is associated with increased risks of fractures, cardiovascular disease, and death. It can be treated medically, but surgical parathyroidectomy is an option when medical treatment is not helpful or when associated with complications like renal bone mineral disease and calciphylaxis or calcific uraemic arteriolopathy[6]. Renal secondary hyperparathyroidism results from low levels of vitamin D, inability to activate vitamin D, low serum calcium, and diminished renal excretion of phosphate[7]. Continued excess PTH secretion will ultimately cause raised calcium levels. Subtotal and total parathyroidectomy with auto-transplantation are recognised surgical options, in case of unsuccessful medical treatment, followed by renal replacement therapy[7,8]. Surgery, is usually the mainstay of treatment in tertiary hyperparathyroidism in very advanced kidney failure[9].

Brown tumour of hyperparathyroidism caused by increased osteoclastic activity and fibroblastic proliferation (Osteitis Fibrosa Cystica) is histologically a Giant cell rich lesion[10]. Brown tumours in longstanding hyperparathyroidism are seen in 3 - 4% of primary hyperparathyroidism and in 1.5% of secondary hyperparathyroidism. They involve the ribs, clavicles, pelvis, femur, and jaw bones – with the mandible more commonly affected than the maxilla[11]. No exact statistical data is available of the association of this rare tumour with tertiary hyperparathyroidism. There was no response to subtotal parathyroidectomy with lowering of PTH and the patient required maxillary surgery.

The patient is currently on Levothyroxine, with a target to keep TSH suppressed (N: 0.35 - 5.5 mU/L) and is also managed in accordance with the the six goals of management of chronic hypoparathyroidism[12]:-

- Ensure that the patient does not have the symptoms of hypocalcaemia.
- Improve the patient's QoL (Quality of Life).
- Maintain serum calcium levels in the low-normal range.
- Keep serum phosphate within the normal range.
- Keep total calcium-phosphate product under 4.4 $mmol^2/l^2$ (55 mg^2/dL^2).
- Prevent hypercalciuria.

The patient remains on haemodialysis with future option of renal transplantation.

Conclusion

This is an interesting case; thyroid cancer was detected while investigating for raised PTH in renal impairment (requiring total thyroidectomy), a rare Brown tumour of jaw was associated with no improvement after lowering of PTH following subtotal parathyroidectomy, requiring maxillary surgery.

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