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Tertiary hyperparathyroidism – location dilemma

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ABSTRACT

Renal failure is associated with numerous complications including cardiovascular, dermatological, neurological, surgical and endocrine. Hypovitaminosis D induces secondary hyperparathyroidism and long term effects are represented by autonomous stimulation of the parathyroid glands (tertiary hyperparathyroidism). Fail of PTH (parathyroid hormone) levels control through vitamin D replacement makes necessary a surgical intervention because of the risk of chronic complications in addition to the general morbidities caused by chronic kidney disease including osteoporosis. Our aim is to present a case of an adult woman with a very long history of renal failure complicated with tertiary hyperparathyroidism and osteoporosis. The clue of the case is the difficult localisation of PTH source after total parathyroidectomy was previously done in order to remove it and timing of re-intervention. There is a challenge to adequately locate the parathyroid remnants after a prior glands removal and a skilled surgeon is still the best "tool". However, the risk of surgery in a cases with multiple complications is very high so it is preferable a pre-operatory localisation. The neck ultrasound is the most accessible tool offering a good accuracy if there is no mediastinal localisation and also the combination with parathyroid scintigram increases the rate of detection.

Keywords: parathormone, hyperparathyroidism, renal failure

Abbreviations
BMD = bone mineral density
DXA = Dual-Energy X-Ray Absorptiometry
PTH = parathormone
SD = standard deviation

INTRODUCTION

Renal failure is associated with numerous complications including cardiovascular, dermatological, neurological, gastrointestinal, surgical and endocrine (1,2). The lack of renal function causes a deficiency of parathormone (PTH) action at the level of kidney cortex thus the activation of vitamin D which normally goes through hydroxylation as final step does not take place anymore (3,4). Hypovitaminosis D induces secondary hyperparathyroidism and long term effects are represented by autonomous stimulation of the parathyroid glands (tertiary hyperparathyroidism) (3-7). Vitamin D supplements of active type fail to success and parathyroid surgery remains a feasible option (5-7). Even small remnants of the parathyroid glands either eutopic or ectopic may be intensely active due to chronic stimulation and they might produce large amounts of PTH which are not correlated with the

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anatomical size of the adenoma (8). Fail of PTH levels control through vitamin D replacement makes necessary another surgical intervention because of the risk of chronic complications in addition to the general morbidities caused by chronic kidney disease including osteoporosis (9,10). As useful tools for the practitioners in order to evaluate to bone status we mention the bone turnover markers, the levels of bone hormones like PTH as well as central DXA (Dual-Energy X-Ray Absorptiometry) (11-13).

AIM

Our aim is to present a case of an adult woman with a very long history of renal failure complicated with tertiary hyperparathyroidism and osteoporosis. The clue of the case is the difficult localisation of PTH source after total parathyroidectomy was previously done in order to remove it.

MATERIAL AND METHOD

This is a case report. Hormonal and imaging data are introduced.

CASE REPORT

This is 63-year old Caucasian female diagnosed with chronic kidney disease more than 15 years ago. She is under haemodialysis soon after the diagnosis was established. She spontaneously went through menopause by the age of 48 years. For the last decade she was also confirmed with osteoporosis and she was treated with oral bisphosphonates. Also she had the four parathyroid glands removed a few years after starting haemodialysis. She continued with vitamin D of different regimes in the mean time. She associates chronic ischemic cardiac disease, atrial fibrillation, and high blood pressure under adequate therapy.

Two years ago the patient's assessment indicated a bone mineral density (BMD) improvement with a relative control of blood mineral metabolism: a PTH level of 480 pg/ml (normal: 16-65 pg/ml) and a 25-hydroxivitamin D of 34 ng/ml (normal: 30-100 ng/ml), and alkaline phosphatase of 412 U/l (normal: 40- 180 U/l). At that point she continued with 1 μg of active vitamin D and drug holiday was decided for risendronate. No visualisation of the parathyroid remnants was possible though anterior cervical ultrasound, cervical and mediastinal computed tomography, parathyroid scintigram.

The next year PTH dramatically increased to 1912 pg/ml (normal: 15-65 pg/ml) as well as bone turnover markers: CrossLaps (for resorption) of 5.4 ng/ml (normal: 0.33-0.782 ng/ml), osteocalcin (for formation) of 300 ng/ml (normal: 15-46 ng/ml). DXA showed a L2-4 lumbar BMD of 0.877 g/sqcm, T-score of -2.7 SD (a -2.3 SD was registered one year before) and Z-score of -1.6 SD; femoral neck BMD of 0.812 g/sqcm, T-score of -1.6 SD, Z-score of -.0.5 SD, total hip BMD of 0.825 g/sqcm, T-score of -1.4 SD, Z-score of -0.6 SD; third distal left radius BMD of 0.418 g/sqcm, T-score of -4.1 SD, Z-score of -3.1 SD. The doses of vitamin D were increased and risendronate was re-started. No location of the parathyroid glands was done by ultrasound or computed tomography.

Currently, one year later, PTH levels are still high of 1931 pg/ml (normal: 15-65 pg/ml), CrossLapss had a small decrease to 4.7 ng/ml (normal: 0.33-0.782 ng/ml) while osteocalcin had the same values; a total serum calcium of 10.3 mg/dl (normal: 8.5-10.2 mg/dl), and phosphorus of 7.1 mg/dl (normal: 2.3-4.7 mg/dl) was assessed. BMD improved to each central site: L2-4 lumbar BMD of 0.933 g/sqcm, T-score of -2.2 SD and Z-score of -0.8 SD; femoral neck BMD of 0.874 g/sqcm, T-score of -1.2 SD, Z-score of 0.2 SD, total hip BMD of 0.885 g/sqcm, T-score of -1 SD, Z-score of 0.1 SD; third distal left radius BMD of 0.432 g/sqcm, T-score of -4 SD, Z-score of -2.9 SD. Parathyroid scintigram Tc99 identified a left inferior parathyroid adenoma superior to sternum area for the first since the tertiary hyperparathyroidism relapsed after first parathyroid surgery (Figure 1). The lesion of 1 cm (centimetre) was also confirmed at anterior cervical ultrasound at the same level and then surgically removed with a lowering of PTH levels (Figure 2).

DISCUSSION

There a challenge to adequately locate the parathyroid remnants after a prior glands removal and a skilled surgeon is still the best "tool" (14). However, the risk of surgery in a cases with multiple complications as here is very high so it is preferable a pre-operatory localisation. That is why the surgery was postponed in this situation. The neck ultrasound continues to be the most accessible tool offering a good accuracy if there is no mediastinal localisation (15). One study on 810 patients showed that eutopic parathyroids with abnormal pattern are more likely to be inferior as this was the case (16). Yet in cases with renal failure and persistent hyper-

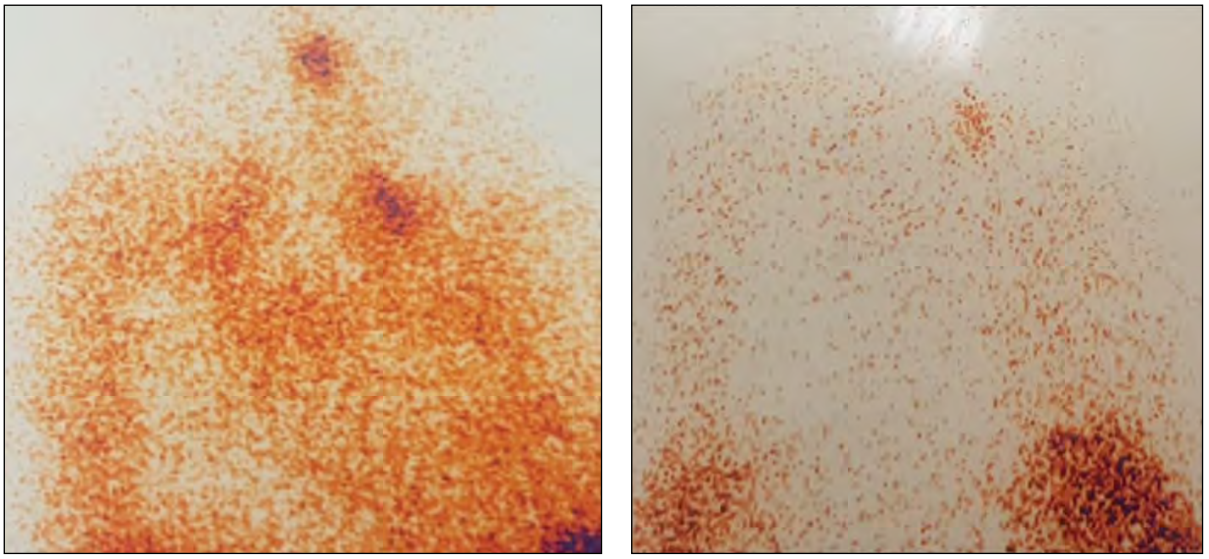

FIGURE 1. *Parathyroid scintigram Tc99 (Technetium) identified a left inferior parathyroid adenoma superior to sternum area (different timing)*

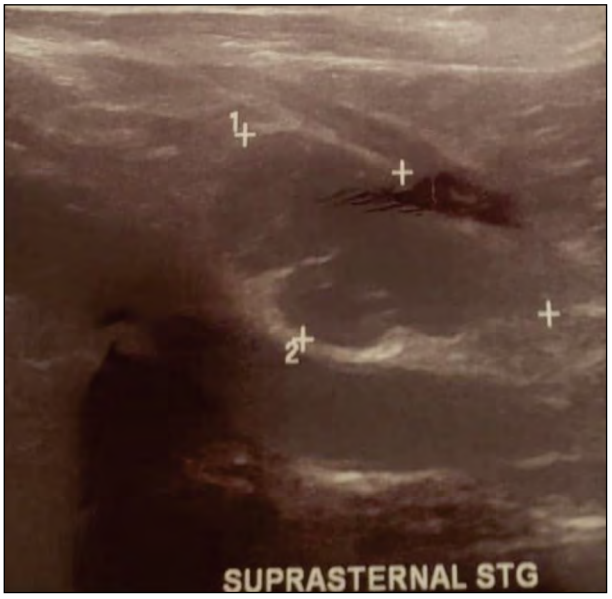

FIGURE 2. *Cervical ultrasound identifies a parathyroid adenoma causing tertiary hyperparathyroidism*

parathyroidism the re-intervention decision is delicate and a close selection needs to be done (17). In this particular situation the values of PTH are extremely high as seen here in addition to increased bone turnover profile reaching levels that are completely different to usual cases of primary hyperparathyroidism or primary osteoporosis (18,19). Moreover, even the patient had extremely high PTH serum calcium levels were controlled through haemodialysis (20).

CONCLUSION

The reoperation of a patient with tertiary hyperparathyroidism and a long standing history of parathyroidectomy are based on a rigorous selection and the pre-operatory location of the parathyroid adenoma is crucial even challenging.

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