CLINICAL CASE

RE-OPERATIVE SURGERY FOR RECURRENT PRIMARY HYPERPARATHYROIDISM ASSOCIATED WITH OLIGOMENORRHEA

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Abstract

Recurrent primary hyperparathyroidism is characterized by typical symptoms and biochemical recurrence of hypercalcemia after more than 6 months of normal calcium levels after surgery. We report the case of a 39-year-old female patient presenting with menses disturbances who was diagnosed with primary hyperparathyroidism caused by a left inferior parathyroid adenoma at the age of 35. Postoperative 6-month follow-up showed normalization of biochemical and hormonal profiles, with significant improvement of clinical symptoms, dominated by muscle weakness, weight loss and oligomenorrhea. The 18-month follow-up showed elevated PTH and serum calcium levels. Imaging confirmed recurrence of primary hyperparathyroidism by highlighting a right upper parathyroid adenoma. Surgery was performed again and no major incident was seen. The particularity of this case consists in the recurrence of primary hyperparathyroidism in a young patient with no family history of the disease due to asynchronous parathyroid adenomas that were successfully removed in a female patient who in addition to classic complications such as calyceal microlithiasis and osteoporosis presented oligomenorrhea which was resolved spontaneously after the correction of hypercalcemia.

Keywords*: parathyroidectomy, recurrent hyperparathyroidism, hypercalcemia, oligomenorrhea*

Introduction

Primary hyperparathyroidism is the most common benign cause of hypercalcemia. In 85% of cases primary hyperparathyroidism is caused by a benign solitary adenoma, the remaining 15% being due to diffuse hyperplasia of the parathyroid glands [1,2]. Surgical removal of the adenoma or the hyperplastic glands will provide cure in 95% of cases, with a recurrence rate of maximum 30% [3]. Persistence of primary hyperparathyroidism can be defined as the persistence of hypercalcemia within 6 months after surgery [4]. Recurrent hyperparathyroidism is characterized by recurrence of hypercalcemia after more than 6 months postoperatively [5]. The reported incidence is up to 3% and it has been described both in familial forms and in sporadic disease [6]. The most common causes for recurrent

sporadic hyperparathyroidism are the inadequate resection of parathyroid tissue in case of parathyroid hyperplasia, incomplete resection followed by local relapse of parathyroid adenomas or the occurrence of a second parathyroid adenoma with a different location [7]. Accuracy of preoperative localization studies is essential for the success of re-operative surgery.

Case report

We present the case of a 39-year-old female patient who presented at the age of 35 oligomenorrhea followed by amenorrhea. Then she was admitted for lower back pain, weight loss (6 kg in 2 months), headaches, fatigue, muscle weakness, nausea, polyuria. The patient had previous history of kidney stones, diagnosed 7 years prior to admission and osteoporosis confirmed on DXA (Dual X-Ray Absorptiometry) 4 before admission.

The biochemistry and endocrine tests confirmed primary hyperparathyroidism(Table 1). The anterior cervical ultrasound showed a left inferior parathyroid nodule (Figure 1). The 99mTc-SESTAMIBI scan revealed a solitary parathyroid adenoma located in the left lower parathyroid gland.

The patient underwent selective parathyroidectomy for left inferior parathyroid tumour. During surgical procedure bilateral cervical exploration was associated with complete resection of the left lower parathyroid. The recovery went well and the patient was discharged within 4 days.

The pathological report confirmed a parathyroid adenoma. Postoperatively she was prescribed calcium and vitamin D supplements for 3 months in order to correct potential symptoms of hypocalcemia. The PTH (parathormone) was normal immediately after surgery.

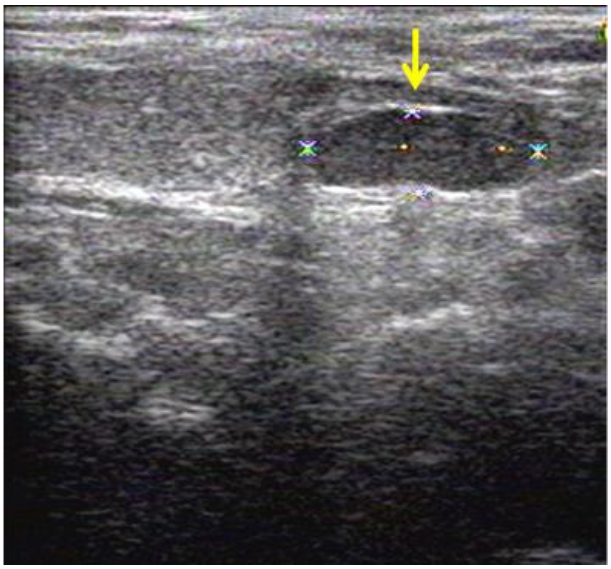

Figure 1 - Anterior cervical ultrasound: left inferior parathyroid nodule (yellow arrow)

Parameter	Preop. I	Postop. I (6 M)	Postop. I (18 M)	Postop. I (24 M)	Preop. II	Postop. II (6 M)	Reference Range
PTH (parathormone)	107.6	42	83.9	97.5	100.7	36.8	15-65 pg/ml
total serum calcium	10.7	9.5	10.5	11	11.2	9.2	8.4-10.5 mg/dl
ionized serum calcium	4.4	4.2	4.46	4.5	4.6	4.1	3.82-4.82mg/dl
24-hours urinary calcium	500.4	194.6	388.8	887.6	997.5	188.4	100-300 mg/24-h
plasma fasting glucose	85	92	89	90	83	88	70-110 mg/dl
serum prolactin	236	132	456	354	520	420	127-637µUI/ml
serum 25-OH vitamin D	110	76	89	110	123	99	22-111pg/ml
creatinine	0.58	0.62	0.68	0.8	0.67	0.7	0.57-1.11 mg/dl

Table 1 - Biochemical and hormonal parameters in a young female who underwent surgery twice for primary hyperparathyroidism due to asynchronous parathyroid adenoma

The 6-month follow-up showed normalization of PTH, total and ionized calcium levels, with significant improvement of clinical symptoms: weight gain (a body mass index of 20.82 kg / sqm), absence of fatigue, regular menses. 18 months after initial surgery the patient presented recurrence of menstrual disorders, polyuria, muscle weakness, emotional lability and elevated serum calcium and PTH levels were found that were consistent with recurrent primary hyperparathyroidism (Table 1).

Cervical sonography described the presence of an extracapsular nodule of 8.3 by 2.5 mm diameter, located at the upper pole of the right thyroid lobe. CT (computer tomography) scan as well as 99mTc - SPECT/CT (50+450MBq) imaging confirmed the presence of an 8 by 3 mm parathyroid adenoma located at 35 mm distance from the upper pole of the right thyroid lobe and hyperfunctional thyroid (Figure 2).

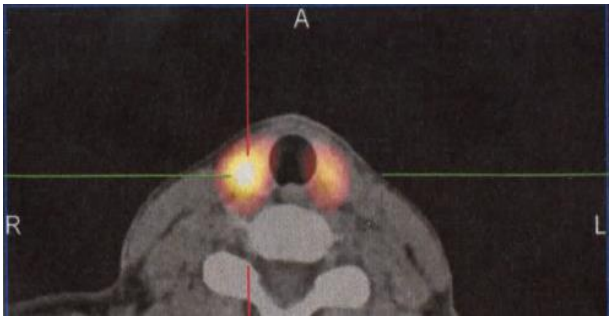

Figure 2 - 99mTc-sestamibi scan highlighting a parathyroid adenoma located in the upper pole of the right thyroid lobe.

Thus three years after initial surgery the patient underwent right upper parathyroidectomy and right thyroid lobectomy. PTH levels 1 hour after surgery decreased to normal and confirmed the complete removal of the lesion. The clinical evolution during hospitalization for surgery associated no side effects and the patient was discharged within a week. The pathological examination revealed a parathyroid adenoma (that was asynchronous to the first one).

Currently the patient is asymptomatic presenting with normal PTH and serum calcium levels. She is undergoing thyroid replacement therapy with 50 mcg levothyroxin per day and antiresorbtive treatment with weekly alendronate together with vitamin D supplements for bone health.

Discussions

Recurrent primary hyperparathyroidism is characterized by typical symptoms and biochemical recurrence of hypercalcemia after 6 to 12 months postoperatively. Relapse is more frequent in familial forms of hyperparathyroidism, particularly multiple endocrine neoplasia syndrome type 1 (MEN 1) [8]. Normal prolactin and plasma glucose levels, the presence of a solitary left lower parathyroid adenoma on 99mTc-sestamibi scan and negative family history ruled out MEN 1 as the cause of recurrent hyperparathyroidism. Neither type 2A of MEN syndrome was confirmed in our case. The recurrence of hypercalcemia just 18 months after initial surgery raised the question whether the right upper and left lower parathyroid adenomas coexisted or a secondary malign cause of high cause is involved. In this particular situation the PTH levels are suppressed [9,10]. Recurrence of primary hyperparathyroidism due to coexistence of multiple adenomas has been described in literature [11]. Inadequate intraoperative exploration may fail to identify a contra-lateral parathyroid microadenoma which only leads to the resection of the lesion described on MIBI scan. In addition small adenomas or those with low mitochondrial content may show rapid washout of the radiotracer, and thus escape detection [12]. In our case recurrence of hyperparathyroidism was due to the development of a new parathyroid adenoma located at a distance from the initial lesion.

Re-operative surgery presents technical difficulties and it is associated with higher morbidity rates. Postoperative fibrosis can make it difficult to identify parathyroid tissue or the recurrent laryngeal nerves [13]. For this reason preoperative localization of the lesion is essential for the success of re-operative surgery. In this case the lesion responsible for the recurrence of hyperparathyroidism was initially identified by ultrasound and CT scan, and later confirmed by 99mTc-SPECT imaging.

In order to ensure that surgery is successful PTH levels are measured intra-operatively or at least the day after surgery. If intra-operative or postoperative PTH measurements are not routinely required for initial surgery they are extremely useful in case of recurrent

hyperparathyroidism. [14]. In this female case PTH levels dropped to 22 pg/ml 4 hours after surgery compared to 100.7 pg/mL preoperatively. When imaging techniques are unable to identify the lesion, the guidelines recommended preoperative methylene blue and sestamibi administration with subsequent use of intraoperative radioprobe [15]. In our case this technique was unnecessary due to preoperative localization of the lesion using ultrasonography, CT scan and parathyroid scintigraphy.

Apart from the data provided by the preoperative imaging techniques, the experience of the surgeon is essential in the case of recurrent hyperparathyroidism. Depending on the information obtained during initial surgery, intra-operative strategy can decide the further course of the disease. In this case the surgical team decided to perform right thyroid lobectomy and ligation of the inferior thyroid artery which supplied the right inferior parathyroid gland. The adequate control of the disease is supported by improvement of DXA scan T-scores (up to the level of lumbar Z-score of -1.9 SD, femoral neck Z-score of -0.8 SD), return of regular menses and stationary left renal microlithiasis.

Conclusion

The particularity of this case consists in the recurrence of primary hyperparathyroidism in a young patient with no family history of the disease due to asynchronous parathyroid adenomas that were successfully removed in a female patient who in addition to classic complications such as calyceal microlithiasis and osteoporosis presented oligomenorrhea which was resolved spontaneously after the correction of hypercalcemia.

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