CASE REPORT

Spontaneous regression of hypercalcemia in a patient with primary hyperparathyroidism and prolactinoma

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ABSTRACT. We describe a unique case of spontaneous resolution of hyperparathyroidism in a lady with combined parathyroid adenoma and prolactinoma, raising the possibility of underlying multiple endocrine neoplasia (MEN) 1 syndrome. We also discuss the mechanism and natural history of such spontaneous remission.

INTRODUCTION

Primary hyperparathyroidism is a common endocrine condition characterized by excess secretion of parathyroid hormone (PTH) manifesting as hypercalcemia. The condition is often sporadic, caused by a solitary adenoma of the parathyroid gland although it also exists in inherited forms as in multiple endocrine neoplasia (MEN) or Familial hypocalciuric hypercalcemia (1). Definitive management for a parathyroid adenoma causing significant hypercalcemia is surgery. Clinical remission of primary hyperparathyroidism due to spontaneous infarction or hemorrhage of a parathyroid adenoma has been rarely described previously (2-5). We describe a unique case of spontaneous resolution of hyperparathyroidism in a lady with combined parathyroid adenoma and prolactinoma, raising the possibility of underlying MEN 1 syndrome. We also discuss the mechanism and natural history of such spontaneous remission.

CASE REPORT

A 30-yr-old Caucasian lady first presented in 1989 with left ureteric colic secondary to a small stone, which resolved spontaneously. She subsequently presented in 1995 to the Gynecologists with oligomenorrhea. Upon investigations then, she was found to have elevated prolactin levels at 2140 mU/l (65-490 mU/l) and a magnetic resonance imaging (MRI) scan of the pituitary fossa was consistent with a micro adenoma. The rest of her gynecological and pituitary function tests were normal. She was commenced on treatment with dopamine agonists with good response both clinically and biochemically. She re-presented to her general practitioner in 1996 with back pain when a routine lumbar spine X-ray commented on changes suggestive of renal osteodystrophy and bilateral nephrocalcinosis. She was therefore referred for specialist management. Routine biochemistry revealed significant hypercalcemia - corrected Ca²⁺ 3.29 mmol/l (2.0-2.6 mmol/l) with elevated alkaline phosphatase - 2748 IU/l (80-330 IU/l) and normal serum creatinine - 112 μmol/l (60-120 μmol/l). A serum PTH was significantly elevated at 858 ng/l (10-60 ng/l). 24-h urinary estimation of calcium was elevated at 11.6 mmol (<6 mmol).

The etiology of her primary hyperparathyroidism was worked up further. An ultrasound examination of the neck showed a 1 cm-echogenic adenoma in the right lower parathyroid, which also demonstrated an abnormal uptake on parathyroid scintigraphic (sestaMIBI) examination. Other parathyroids were not visible. The combination of parathyroid adenoma and pituitary adenoma with hyperprolactinemia raised the possibility of underlying MEN 1 syndrome. Further investigations showed normal serum levels of calcitonin and gastrin and urinary levels of catecholamines and 5-HIAA. There was a family history of recurrent renal stones although neither the etiology of the same nor the presence of features suggestive of MEN 1 syndrome were present. She then presented to her general practitioner in 2003 with back pain and a routine lumbar spine X-ray showed evidence of osteopenia.

Key-words: Hypercalcemia, primary hyperparathyroidism, autotrophic resection, prolactinoma, multiple endocrine neoplasia.

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in them could be ascertained. Sequence analysis of exons 2-10 in our patient revealed no evidence of germline mutation (20% false negativity). In view of significant and persistent hypercalcemia, she was scheduled to have a parathyroidectomy. Meanwhile, 2 weeks prior to the scheduled date of surgery, she had presented to an Accident and Emergency department with a minor fall when she was found to have a pathological fracture of the mid-shaft of right humerus which also showed cystic changes consistent with parathyroid bone disease. This was managed surgically with no intra- or post-operative complications. Surprisingly, the serum calcium was normal (Corrected Ca^2+ 2.37) during this admission in 1997 and this was confirmed on several occasions subsequently. Plasma PTH level also fell (255 ng/l) though it was still significantly elevated. Dual energy X-ray absorptiometry (DEXA) studies of the femoral neck (T score=+1.4, Z score=+1.4), and lumbar spine (T score=-0.5, Z score=-0.6) were surprisingly within normal range. Upon follow-up (Fig. 1), the serum calcium remains normal to date (5 yr since remission), the serum PTH and alkaline phosphatase completely normalised, the nephrocalcinosis on plain X-ray remains stable and the serum creatinine remains normal. Repeat ultrasound examination of her neck revealed the previously echogenic adenoma to have changed to a low attenuation lesion with calcification.

DISCUSSION
We present a 30-yr-old lady who had a parathyroid adenoma and a pituitary microprolactinoma, in whom regression of the primary hyperparathyroidism with normalisation of serum calcium and PTH levels was observed in the absence of specific medical intervention. We presume she had a spontaneous infarction of the parathyroid adenoma. Spontaneous remission secondary to either infarction or hemorrhage of parathyroid adenoma has been infrequently recognised in patients with primary hyperparathyroidism (2-5). Inducing such infarction by radiological embolisation has also been successfully used as a temporary therapy for hyperparathyroidism (6). While hemorrhagic necrosis usually manifests with pain, swelling and tenderness in the lower neck, infarction may or may not present with pain. The exact cause of such spontaneous hemorrhage or infarction remains unknown although a larger adenoma is believed to be prone to ischemic insult (2). The natural history and the course of events that follow such spontaneous remission is variable though it is likely to consist of three phases. First, the massive release of PTH transiently exacerbates the hypercalcemia (4) followed by a stage of hypocalcemia, which sometimes can be acute and manifest with tetany (5). The sudden cessation of PTH secretion, the inability of the remaining parathyroid glands to respond appropriately due to chronic suppression and the hungry bones phenomenon all contribute to this hypocalcemia. In the third stage, remission is achieved, although sometimes it is partial (3).

Other potential causes for apparent normocalcemia in patients with primary hyperparathyroidism include physiological fluctuations (7), concomitant Vitamin D deficiency, hypoalbuminemia, hypomagnesemia and pancreatitis although these were not relevant to our case. Our patient is likely to have had a spontaneous remission of her parathyroid adenoma and the absence of pain and the changes observed on subsequent ultrasound examination point towards an underlying infarction. With multiple endocrine tumours suggesting an underlying MEN 1 syndrome, our patient is unique since such

![Graph showing clinical course of serum calcium, Alkaline phosphatase (ALP) and parathyroid hormone (PTH) levels.](image-url)