

## CLINICAL VIGNETTE

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# Postsurgical Hypoparathyroidism

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### Introduction

The most common complication of bilateral and re-operative thyroid surgery is Hypoparathyroidism.<sup>1</sup> The true incidence of postsurgical hypoparathyroidism is unknown due to variations across different centers, different types of surgery and surgical expertise. Observational studies report transient hypoparathyroidism in up to 20% of patients after surgery for thyroid cancer and permanent hypoparathyroidism occurred in 0.8% to 3.0% of patients after total thyroidectomy.<sup>2,3</sup> It is important to recognize postoperative hypoparathyroidism and promptly administer treatment to minimize the complications from this common condition. We describe a case of postoperative hypoparathyroidism and discuss risk factors, symptoms, signs, complications and treatment.

### Case Presentation

A 27-year-old woman with papillary thyroid cancer underwent total thyroidectomy. Prior to the surgery, her calcium was 9.7 mg/dl (8.6 mg/dl to 10.3 mg/dl) and vitamin D was 45 ng/ml (20ng/ml -50ng/ml). Her intra operative PTH (parathyroid hormone) was 8 pg/ml. On post-operative day one, her calcium was 8.0 mg/dl. She experienced mild numbness and tingling which resolved with oral therapy. She was discharged home with calcium carbonate 1500mg in 3 divided dosage and calcitriol 0.25mcg twice a day. Her calcium and calcitriol were gradually tapered off. However, four weeks after the surgery, she developed paresthesia of the face, neck, hand and feet. Her physical exam included negative Chvostek's and Trousseau signs. Repeat calcium was 8.3 mg/dl, and ionized calcium was 1.07 mmol/l (1.09-1.29 mmol/L). Calcium carbonate 500mg three times a day was reinitiated and hypocalcemia symptoms resolved. Calcium levels were monitored weekly and gradually improved. Currently, she is on calcium carbonate 500mg once a day. Calcium level has been maintained between 8.5 to 8.6 mg/dl and PTH remained around 24 pg/ml.

### Discussion

Hypoparathyroidism is defined as intact PTH level; below the lower limit of normal, accompanied by hypocalcemia, hyperphosphatemia, hypercalciuria and symptoms and signs of hypocalcemia.<sup>4</sup> There are different categories of post-operative hypoparathyroidism. Parathyroid insufficiency or relative hypoparathyroidism is presence of hypoparathyroidism symptoms that require medical treatment with normal lab values. Transient and temporary hypoparathyroidism is defined for

symptoms lasting less than six months after surgery while permanent hypoparathyroidism lasts longer than six months.<sup>5</sup>

PTH is regulated by intact calcium level. If the ionized calcium is low, PTH level will increase. PTH stimulates osteoblasts which increases their RANKL expression and allows the differentiation of osteoblasts into osteoclasts. PTH also inhibits the secretion of osteoprotegerin, which is a decoy receptor for RANKL. Osteoclasts cause resorption of bone by dissolution and degradation of hydroxyapatite, releasing calcium and phosphorus into the blood. Circulating PTH targets the distal convoluted tubule and collecting duct, directly increasing calcium reabsorption. PTH decreases phosphate reabsorption at the proximal convoluted tubule and increases the conversion of 25-vitamin D to 1, 25-vitamin D in the kidney. 1, 25-vitamin D increases the absorption of calcium and phosphorus in the intestine. This results in increased levels of ionized calcium levels.<sup>6</sup> During thyroidectomy surgery, mechanical injury can cause hypoparathyroidism disruption of parathyroid arterial supply or venous drainage, with resultant hypocalcemia.<sup>7</sup>

Hypoparathyroidism is associated with many clinical symptoms and signs, ranging from minimal to no symptoms if hypocalcemia is mild, to life threatening seizures, refractory heart failure, or laryngospasm. Paresthesia of the perioral regions and the fingertips, muscle stiffness, cramps, spasms are common.<sup>4</sup> Signs include observed or elicited tetany, and classically a positive Chvostek's sign or Trousseau sign. Cardiovascular signs included prolonged QT interval that can result in Torsade de pointes.<sup>4</sup>

The risks factors for postoperative hypoparathyroidism are bilateral (simultaneous or sequential) thyroid procedures, autoimmune thyroid disease(Graves's disease, chronic lymphocytic thyroiditis), central neck dissection, substernal goiter, low volume thyroid surgeon, prior gastric bypass or other malabsorptive state, simultaneous thyroidectomy and parathyroidectomy, prior central neck surgery and preoperative vitamin D deficiency.<sup>8</sup>

ATA surgical Affairs committee suggested that a PTH value >15 pg/ml measured in adults >= 20 minutes following thyroidectomy would obviate the need for intensive serum calcium monitoring and or calcium supplementation. A level less than 15 pg/ml would suggest an increased risk for acute hypoparathyroidism that might prompt preemptive prescribing

oral calcium and calcitriol and/or serial serum calcium measurement until calcium stability has been confirmed.<sup>8</sup>

The goal of managing hypoparathyroidism is to avoid the symptom and complications of hypocalcemia. Development of acute hypocalcemia after thyroid surgery generally lags behind the decline in the serum PTH level. Patients may have been discharged from the hospital before their calcium reaches nadir, 24 to 72 hours after thyroidectomy. It is important to measure serum calcium, and albumin on the evening of surgery and the next morning and initially weekly. Patients should be alerted to the symptoms, signs, treatment for symptomatic hypocalcemia.<sup>4,8</sup>

Patients whose PTH is <15 pg/ml, serum calcium is <8.5 mg/dl or ionized calcium is < 1.1 mmol/l are considered for postoperative oral calcium supplementation. A regiment of 400-1200 mg per day of elemental calcium (1-3 gram of calcium carbonate) or calcium citrate (2000-6000mg) per day in divided doses is usually used.<sup>9</sup> If patient continues to have symptomatic hypo calcium and a serum calcium level that is declining on measurements or remaining <7 mg/dl, calcitriol 0.25 -0.5mcg twice daily may be added. If serum Magnesium is < 1.6 mg/dl, 400mg of Magnesium Oxide once or twice daily can help. If no improvement in calcium level or severe symptoms, EKG should be performed and intravenous calcium, 1-2 g calcium gluconate in 50ml of 5% dextrose infused over 20 minutes should be given.<sup>8</sup> Once patients are stable on oral therapy to be discharged, calcium level should be monitored. Initially weekly monitoring of urinary and serum calcium and phosphorus are recommended until serum calcium is stable. Once weekly calcium is stable monitoring at three- to six-month intervals is recommended.<sup>4</sup>

Goal of long term management of hypoparathyroidism is to maintain serum calcium within asymptomatic range, avoid significant hypocalcemia or hypercalcemia. Serum calcium should be maintained in the low normal reference range, serum phosphorus should be maintained no higher than the upper normal range and 24 hour urine calcium excretion should be < 7.5mmol/day with calcium-phosphorus product < 55.<sup>10</sup> Most patients require 1500mg calcium carbonate/citrate in two or three divided dosages daily. Calcitriol is recommended as well. Daily Hydrochlorothiazide can be used to prevent hypercalciuria (>150mg/24h).

Long term complications of hypoparathyroidism include nephrolithiasis, nephrocalcinosis, basal ganglia calcification, ectopic soft tissue calcification, renal failure.<sup>11</sup> The FDA has approved recombinant human PTH (1-84) to treat refractory hypoparathyroidism. Due to possible risks of osteosarcoma, only certified healthcare provider can prescribed it.<sup>8</sup> PTH 1-34 is being studied for off label treatment for postoperative hypoparathyroidism.<sup>8</sup>

## Summary

Knowledge of symptoms, signs, complications and treatment for postoperative hypoparathyroidism is very crucial. Once it is diagnosed, prompt therapy should to eliminate the negative impact of postsurgical hypoparathyroidism.

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