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Case Report

Recalcitrant Hypocalcemia: Postsurgical Hypoparathyroidism Exacerbated by a Chyle Leak Treated With Octreotide

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ABSTRACT

Background/Objective: To report a case of recalcitrant post-surgical hypocalcemia caused by hypoparathyroidism complicated by a chyle leak and octreotide use.
Case Report: A man in his 60s with a 4-month history of voice changes, 10-pound weight loss, and a right-sided neck mass presented with difficulty breathing for 1 week. He had a right laryngeal/hypopharyngeal mass, which was biopsied. Pathology results were positive for invasive squamous cell carcinoma. He underwent an extensive neck surgery, including total thyroidectomy. Postsurgical laboratory results revealed serum corrected calcium of 7.6 mg/dL (ref 8.0-10.2 mg/dL) and parathyroid hormone <6.3 pg/mL (ref. 10-65). Despite treatment with calcium carbonate 12 g (elemental) daily, calcitriol and hydrochlorothiazide, his corrected serum calcium levels remained low. Patient also had a chyle leak that was treated with octreotide. Resolution of his hypocalcemia occurred after substitution of calcium carbonate with calcium citrate, cessation of octreotide, and management of the chyle leak.
Discussion: Our patient likely developed recalcitrant hypocalcemia from: 1) postsurgical hypoparathyroidism, 2) a chyle leak, and 3) the use of octreotide. Administration of octreotide to seal the chyle leak most likely decreased gastric acid production and contributed to decrease in absorption of calcium carbonate. Oral calcium citrate may be better absorbed in this case.
Conclusion: Postsurgical hypoparathyroidism can lead to hypocalcemia. This case is unique in that the patient's chyle leak and the use of octreotide contributed to recalcitrant hypocalcemia.

Introduction

Postsurgical hypoparathyroidism is a rare condition with an incidence of 0.8 to 2.3/100 000/person-years, 75% of these cases are transient and 25% are chronic.[1,2] Parathyroid glands may be injured, devascularized, or unintentionally removed during extensive neck surgery, causing hypocalcemia. Severe hypocalcemia may lead to serious sequelae such as ventricular arrhythmias, grand mal seizures, and mental status changes. Consequently, treatment with oral or intravenous calcium replacements, active vitamin D (calcitriol), magnesium repletion, or hydrochlorothiazide, are vital when parathyroid hormone (PTH) is absent or insufficient. We present a unique case of a man who underwent extensive neck surgery and developed recalcitrant hypocalcemia despite usual medical management due to the different contributions of 3 synergistically adverse factors: 1) post-surgical hypoparathyroidism, 2) chyle leak, and 3) octreotide use.

Case Report

A man in his 60s with a 4-month history of voice changes, a 10-pound weight loss, and a right-sided neck mass presented with difficulty breathing for 1 week. Imaging showed a right laryngeal/hypopharyngeal mass. He underwent emergent tracheostomy with direct laryngoscopy for further examination of the mass, which showed cancer invasion into the thyroid gland and the presence of suspicious lymph nodes. The mass was biopsied and pathology results were positive for invasive squamous cell carcinoma with extralaryngeal tumor extension. The surgical team scheduled the

Abbreviations: POD, postoperative day; PTH, parathyroid hormone.

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patient for complete thyroidectomy with bilateral neck dissections, which occurred 2 weeks later after medical management.

On postoperative day (POD) 1, his vital signs were stable. Laboratory results revealed a calcium of 6.2 mg/dL (corrected calcium of 7.3; ref 8.0-10.2 mg/dL), magnesium of 1.2 mg/dL (ref 1.3-1.9 mg/dL) and phosphorus of 5.3 mg/dL (ref 2.7-4.5 mg/dL). His magnesium was repleted. Laboratory values that were low included PTH of <6.3 pg/mL (ref 10-65), 25-hydroxyvitamin D level of 13.1 ng/mL (ref 30-80), and 1,25 (OH)2D of 22.1 (ref 25-40). Other electrolytes and estimated glomerular filtration rate were within normal limits. The patient denied symptoms of perioral numbness, tingling of fingers or toes, or muscle cramping. On POD 3, he was noted to have a chyle leak that was treated with octreotide 100 mg subcutaneously 3 times a day and medium chain fatty acid. The output and contents of the milky chyle drainage were not measured.

Despite treatment with calcium carbonate 12 g (elemental) daily, calcitriol 2 μg daily, vitamin D2 50 000 IU daily and hydrochlorothiazide 12.5 mg daily via gastrostomy tube, his serum calcium levels remained low. The patient required recurrent medical management with intravenous calcium gluconate because the calcium levels would rapidly decrease when intravenous calcium gluconate was stopped (Fig). The patient was treated with his last dose of intravenous calcium gluconate when the lowest calcium concentration was 6.2 mg/dL (corrected calcium of 7.3 mg/dL) on POD 12. His magnesium remained within normal limits. After the patient's calcium levels improved with intravenous calcium gluconate, the patient was administered calcium citrate 1900 mg 3 times daily, as it was presumably better absorbed than calcium carbonate. Around the same time period, his chyle leak resolved and octreotide treatment was stopped. One week afterward, his serum calcium levels improved, and he no longer required intravenous calcium. It was unclear whether the administration of calcium citrate, the resolution of the chyle leak, or the cessation of octreotide mostly contributed to the subsequent improvement in calcium levels because they all occurred around the same time period. His calcium levels remained stable at 9.5 mg/dL on the day of discharge, but his PTH levels remained suppressed throughout his admission. He was discharged with calcium citrate, calcitriol, and cholecalciferol, which were administered through his gastrostomy tube.

Two weeks after discharge, his corrected calcium was low at 7.2 mg/dL, which might be attributed to poor compliance with medications. Eight months after discharge, the PTH level, initially undetectable, was noted to increase but remained low at 5.0 pg/mL (ref: 10-65 ng/mL). Also, his vitamin 25-hydroxyvitamin D levels improved to 31 ng/mL (ref: 30-80). Ten months after discharge, despite chemotherapy and radiation treatments, the patient developed metastatic squamous cell carcinoma to his brain, and was placed under comfort and hospice care. He passed away 1 year after his initial neck surgery.

Discussion

Our patient likely developed recalcitrant hypocalcemia from a combination of 1) postsurgical hypoparathyroidism, 2) a chyle leak, and 3) the use of octreotide. Postsurgical hypoparathyroidism, usually treated with oral or intravenous calcium replacement and calcitriol, was the main cause for hypocalcemia. The commonly used oral preparations for hypocalcemia are calcium carbonate or calcium citrate. If symptoms of hypocalcemia are present and serum calcium levels are <7.0 mg/dL (<1.75 mmol/L) or ionized calcium is below the normal range, elemental calcium infusion should be administered.[1,2] Magnesium should also be restored and normalized if levels are low.

Highlights

- In extensive head and neck surgery, complications may lead to hypocalcemia.
- Chyle leak may exacerbate hypocalcemia, a rare complication of head and neck surgery.
- Chyle leak treatment include pancreatic lipase inhibitors or total parental nutrition.
- Both options decrease lipids in the lymphatics and subsequently, decrease chyle flow.
- Octreotide should be given with calcium citrate for better calcium absorption.

Clinical Relevance

Extensive head and neck surgery may cause chyle leakage, a rare complication that can exacerbate hypocalcemia. Treatment of a chyle leak with octreotide, a somatostatin, decreases gastric acid production, and should be given in conjunction with calcium citrate which does not require gastric acidity for absorption, unlike calcium carbonate.

Despite large doses of calcium carbonate, multiple calcium drip treatments, and calcitriol, our patient's hypocalcemia persisted for 16 days after surgery, suggesting other contributing factors.

The chyle leak caused by thoracic duct injury, a rare complication of head and neck surgery, exacerbated his postsurgical hypoparathyroidism-induced hypocalcemia. Chyle leak is reported in 0.5% to 1.4% of thyroidectomies and 2% to 8% of neck dissections.[3] Chyle is a milky fluid derived from the intestinal lacteals, which returns to the systemic circulation by the thoracic duct. Some components of chyle that can be lost through a leak include lymph, chylomicrons, albumin, triglycerides, cholesterol, electrolytes such as calcium, and fat absorbable vitamins such as vitamin D.[3] In this case, the loss of calcium and vitamin D through the chyle leak most likely exacerbated hypocalcemia. Treatment options for chyle leak include a pancreatic lipase inhibitor to decrease the breakdown of lipids at the duodenum and reduce lipid absorption at the intestines into the lymphatics, or total parental nutrition, which allows lipids to bypass the lymphatic system.[3] Both treatments decrease chyle production and flow. Chyle leak was also managed with a medium-chain fatty acid diet in this case. Medium-chain fatty acids are water soluble and can be absorbed through the portal venous circulation, bypassing the gastrointestinal lymphatic system, which decreases chyle flow.

To help seal the chyle leak in our patient, surgeons used octreotide, a somatostatin analogue. Three decades ago, an animal study showed that somatostatin decreased flow rate in the thoracic duct.[4] Recently, multiple human studies have confirmed that somatostatin can treat thoracic duct injury.[3] However, somatostatin use in our patient most likely contributed to his recalcitrant hypocalcemia. Somatostatin suppresses multiple gastrointestinal hormones like gastrin, decreasing gastric acid production and the rate of gastric emptying. Calcium carbonate, a more affordable oral preparation for calcium replacement, requires gastric acidification for absorption and is most effective when given with food or citrus drinks. The administration of large doses of calcium carbonate was ineffective in our patient, since his gastric acid production had been reduced from the use of octreotide to treat his chyle leak. Intravenous calcium was administered when calcium was severely low. Ultimately,

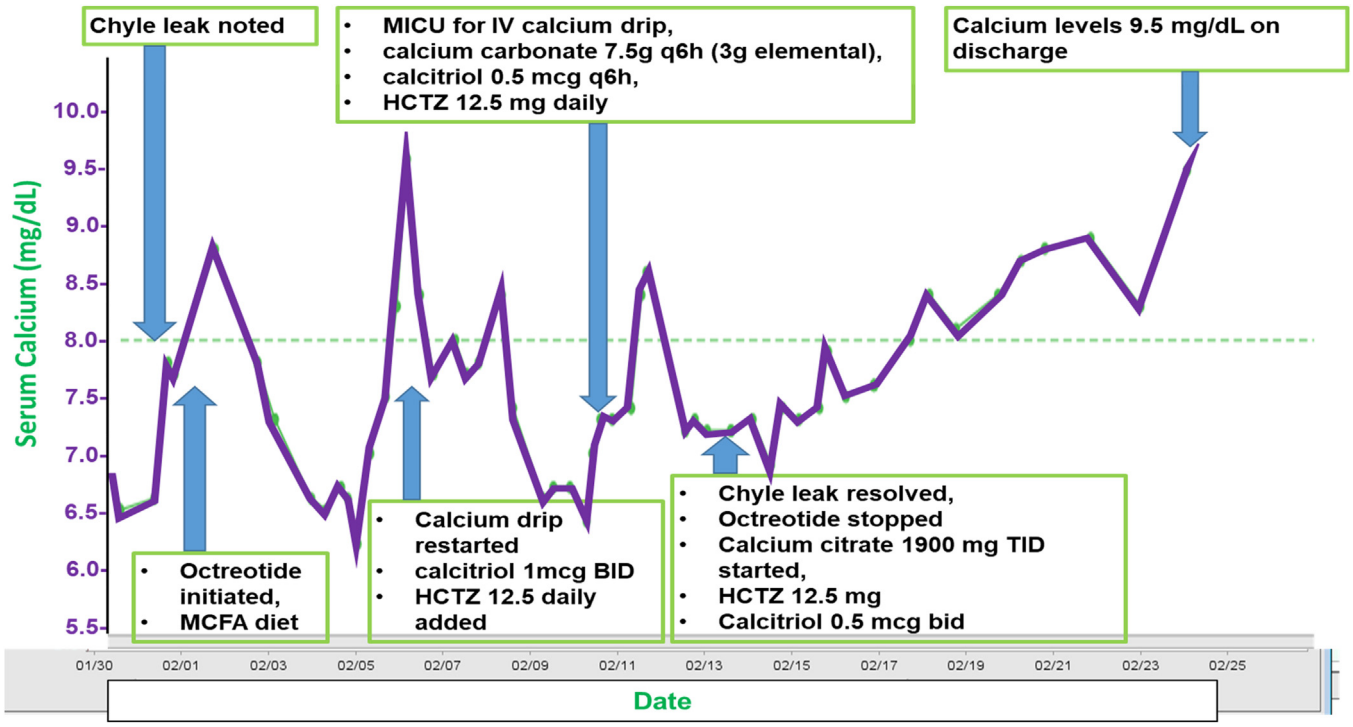

Fig. Course of Inpatient Recalcitrant Hypocalcemia. Hypocalcemia was initially managed with calcium carbonate with the dose up titrated to 1 g (elemental) every 6 hours and calcitriol 0.25 mcg twice a day. Calcium drip was started 01/30 to 02/01 for persistent hypocalcemia. Despite large doses of calcium carbonate, multiple calcium drip treatments, and calcitriol, our patient's hypocalcemia persisted for 16 days after surgery, suggesting other hypocalcemic contributing factors. *HCTZ* = hydrochlorothiazide; *MCFA* = medium chain fatty acid; *MICU* = medical intensive care unit.

switching to calcium citrate was pertinent when intravenous calcium treatment was stopped since gastric acidity is not required for its gastric absorption.

Octreotide itself may potentially decrease plasma calcium. Decreased calcium levels were reported in patients treated with octreotide for acromegaly.[5] In 1 case report, octreotide was effectively used to treat hypercalcemia in a patient with B-cell lymphoma.[6] It is unclear if there are other mechanisms outside of decreased gastric acid production causing octreotide to reduce serum calcium levels; other potential mechanisms need to be further delineated. A previous case report also described a patient with post thyroidectomy chyle leak contributing to hypocalcemia. This patient did not require calcium citrate treatment. Although this patient was also treated with octreotide, it was not discussed as a contributor to hypocalcemia.[7]

Limitations to our case were that the volume and the concentration of calcium, magnesium, and vitamin D in the patient's chyle leak were not known. The chyle and plasma concentrations of electrolytes such as calcium and magnesium are reported to be similar,[8] and chyle leak contributes to electrolyte disturbances.[3] Nonetheless, we believe that a combination of post-surgical hypoparathyroidism, chyle leak, and octreotide use contributed to severe hypocalcemia.

Conclusion

Postsurgical hypoparathyroidism can lead to hypocalcemia. This case is unique in that the patient's chyle leak and the use of octreotide to treat the chyle leak contributed to recalcitrant hypocalcemia. The use of calcium citrate, the resolution of the chyle leak, and the cessation of octreotide contributed to improvement of serum calcium levels.

Disclosure

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Author Contributions

All authors made individual contributions to authorship. BD wrote the case report; MN assisted with data curation; NI, NZ, and LWG critically reviewed the report and made changes; BD and LWG took care of the patient. All authors reviewed and approved the final draft.

Informed Patient Consent for Publication

Signed informed consent could not be obtained from the patient or a proxy but has been approved by the treating institution.

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