

Primary hyperparathyroidism resolution via auto-infarction discovered intraoperatively

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Abstract

Primary hyperparathyroidism is a condition frequently attributed to the excessive secretion of parathyroid hormone (PTH), often stemming from adenoma, hyperplasia, or carcinoma. While the conventional approach to addressing this condition involves surgical intervention, there exist rare instances where spontaneous resolution occurs, typically because of auto-infarction or necrosis of the parathyroid adenoma. In this report, we present the case of a 64-year-old male with hypercalcemia, referred for surgical intervention. Preoperative imaging unveiled a nodular lesion, and intraoperatively, an acutely infarcted adenoma was discovered. Microscopic examination confirmed parathyroid necrosis. Similar cases documented in the medical literature shed light on the potential for non-surgical management options. Factors such as cinacalcet treatment and hypocalcemia-inducing medications have been explored, suggesting alternative approaches to address this condition. Furthermore, cases of spontaneous remission highlight the paramount importance of long-term follow-up in managing primary hyperparathyroidism, ensuring comprehensive and individualized patient care. The awareness of these infrequent occurrences significantly contributes to well-informed decision-making within the medical community.

Keywords: parathyroid, hyperparathyroidism, auto-infarction, adenoma, hypercalcemia

1. Introduction

Primary hyperparathyroidism is the predominant cause of hypercalcemia in the general population, often resulting from excessive secretion of parathyroid hormone (PTH) caused by a single adenoma (>80% of cases), multiple adenomas (6%), hyperplasia (10%), or carcinoma (1%). Diagnosis usually occurs between the third and fifth decades of life, with a higher prevalence among females (1). The conventional approach involves surgical intervention through parathyroidectomy, although in certain cases, such as poor surgical candidates, a conservative approach of watchful waiting may be considered. While exceedingly rare, there have been reported instances of spontaneous resolution of primary hyperparathyroidism due to auto-infarction or necrosis of the adenoma (2-4, 6). In this report, we present a case of an acutely infarcted adenoma discovered intraoperatively, shedding light on previous cases documented in the current medical literature.

2. Case Presentation

The patient is a 64-year-old male with a past medical history of hyperlipidemia and hypertension who was referred to surgery by his endocrinologist for hypercalcemia. Over a period of four years under surveillance, his calcium level remained around 0.56mmol/L with intermittent episodes of hypercalcemia. The patient did not exhibit any symptoms associated with hypercalcemia, such as bone pain, mood swings, nausea, constipation, or kidney stones. However, an annual lab test revealed a calcium level of 0.73mmol/L, leading to the initiation of cinacalcet therapy and a referral for surgery. A sestamibi parathyroid scan did not demonstrate abnormal uptake, and ultrasound performed by the patient's endocrinologist was inconclusive.

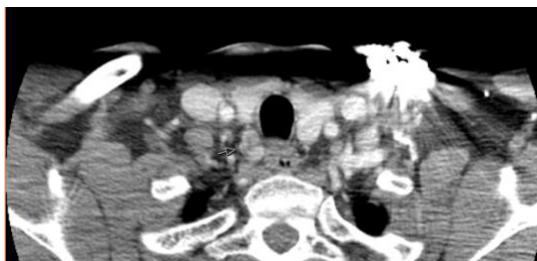


Figure 1. 4D CT demonstrated a 1.6 cm nodular lesion located to the right of the tracheal esophageal groove.

Repeat ultrasound at surgery clinic showed a hypoechoic area that appeared more vascular in etiology. A 4D CT scan was ordered, which revealed a 1.6 cm nodular lesion located to the right of the tracheal esophageal groove (Fig. 1). The lesion exhibited central hypo-enhancement, particularly evident in the arterial phase. Subsequently, the patient was scheduled for a parathyroidectomy.

The parathyroidectomy was performed on 1/6/2022, two months after initial referral and four months after the initiation of cinacalcet. Prior to surgery, the patient's last PTH was 19.1pmol/L on 11/6/2021 and calcium was 0.49mmol/L on 12/23/2021 following cinacalcet treatment (Table 1).

Table 1: Patient preoperative labs

	Results (reference)
Calcium (mmol/L)	0.38 (0.47–0.58)
Ionized calcium (mmol/L)	0.95 (1.14–1.29)
PTH (pmol/L)	11.66 (0.64–7.11)
T ₄ L (ng/dl)	0.8 (0.7 – 1.7)
TSH (UI/ml)	1.5 (0.4 – 4.0)
ALP (U/L)	847 (40–160)
Chloride (mEq/L)	106 (98–107)
Magnesium (mEq/L)	2.0 (1.6–2.6)
Creatinine (mg/dl)	0.4 (0.7–1.0)
LH (mUI/ml)	2.0 (0.3 – 13)
FSH (mUI/ml)	14.0 (13 – 30)
Prolactin (ng/dl)	14.0 (<25.0)
Plasma cortisol (µg/dl)	6.4 (5.0 – 20.0)
25-Hydroxyvitamin D (ng/ml)	11.0 (15.0 – 80.0)
1,25(OH) ₂ D (pg/ml)	210 (15.0 – 60.0)

Intra-operatively, extensive fibrosis was observed surrounding the right-sided gland. A large vessel supplying the gland was ligated and divided, and the gland was removed and sent for frozen section. Intraoperative parathyroid hormone levels decreased from 9.76 pmol/L to 8.91 pmol/L to 8.17 pmol/L at 5, 10, and 15 minutes, respectively. Pathology interpreted the frozen section as infarcted parathyroid tissue. The remainder of the procedure was uneventful, and the patient was discharged home on the same day.

Microscopic examination of the removed tissue revealed near total parathyroid necrosis

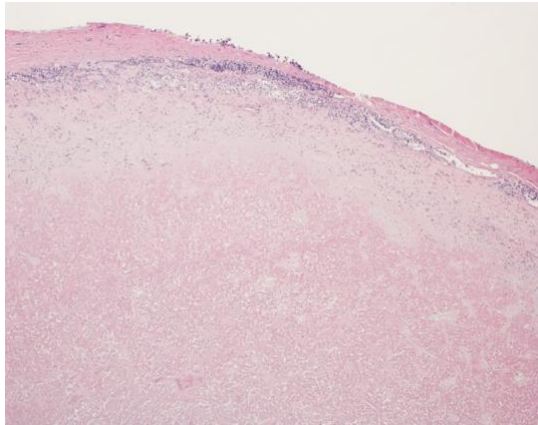


Figure 2. Largely infarcted parathyroid gland with central necrosis that surrounded by fibrosis and

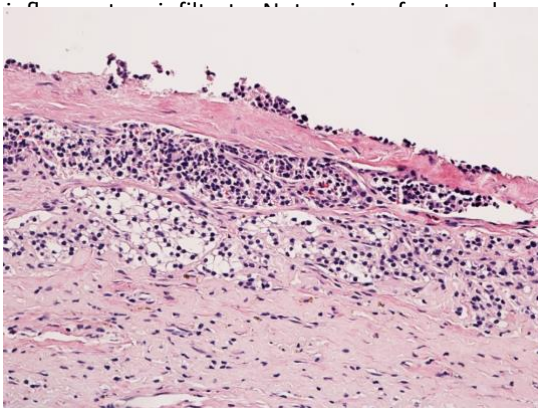


Figure 3. Hypercellular water clear cells (black arrow) separated by a thin fibrous capsule from compressed conventional parathyroid chief cells. Note adjacent fibrosis and hemosiderin deposits.

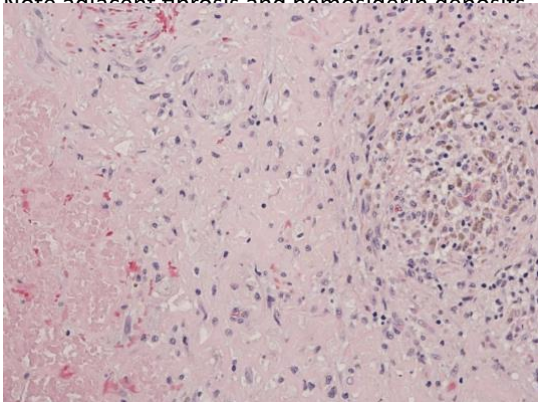


Figure 4. Fibrous wall containing hemosiderin-laden macrophages, lymphocytes, and multinucleated giant cell adjacent to acellular debris and hemorrhages consistent with parathyroid auto infarction (H&E stain, $\times 20$).

with increased fibrosis, hemosiderin deposits, macrophages, lymphocytes and multinucleated giant cells. A rim of proliferating monomorphic chief cells with abundant water-clear cytoplasm was noted around the necrosis. A small portion of

compressed normal parathyroid tissue was visible at the edge. The findings were consistent with auto-infarction of a parathyroid adenoma (Fig. 2, 3, 4). At the patients two month follow up, his calcium was measured as 0.51mmol/L.

3. Discussion

Although relatively rare, there have been several reported cases in which a parathyroid gland spontaneously hemorrhages, resulting in infarction and subsequent resolution of primary hyperparathyroidism and associated symptoms. Liu et al. documented such a case involving a 47-year-old male who presented with hypercalcemic crisis and underwent surgical treatment (4). Postoperative pathology revealed intracystic hemorrhage in both adenomas. It is mentioned in this case that hemorrhage of parathyroid adenomas may be caused by rapid tumor growth with an insufficient blood supply to the tumor. In this case, the adenomas were of significant size at 5 x 3 x 3.5 cm on the right and 5.5 x 4 x 3.5 cm on the left. Although the presentation was more acute compared to our patient, both cases involved an infarcted gland found postoperatively.

In a separate study by Novodvorsky et al., two cases of parathyroid auto-infarction were described (6). This study was unique in that one was managed surgically and the other conservatively, indicating the possibility of non-surgical approaches in such patients. The first case involved a 51-year-old man with primary hyperparathyroidism (PHPT) who had elevated calcium (3.11 mmol/L) and parathyroid hormone (PTH) levels (26.9 pmol/L) and was referred for parathyroidectomy. Repeat biochemistry tests four weeks later prior to surgical intervention showed normal adjusted calcium and reduced PTH levels. Serial ultrasound imaging demonstrated a decrease in the size of the parathyroid lesion from 33 mm to 17 mm. Twenty months later, following recurrence of hypercalcemia, the patient underwent neck exploration and resection of an enlarged right inferior parathyroid gland. Histology revealed increased fibrosis and hemosiderin deposits in the parathyroid lesion which was consistent with auto-infarction. In the second case, a 54-year-old woman presented with hypercalcemia (4.58 mmol/L) and was treated with intravenous fluids and pamidronate. Eight days later, she developed symptomatic hypocalcemia (1.88 mmol/L) accompanied by a significant decrease in PTH levels (17.6 pmol/L) in the setting of severe vitamin D deficiency. MRI of the neck

revealed a 44 mm cystic parathyroid lesion. Long term follow-up at 18 months revealed she had remained normo-calcemic. The authors proposed that auto-infarction may have occurred due to the use of a bisphosphonate and resulting hypocalcemia. While the exact etiology of auto-infarction remains unknown, our case highlights the potential occurrence of auto-infarction in the setting cinacalcet treatment and non-surgical management. We theorize that the acute reduction in gland size induced by cinacalcet, leading to decreased PTH synthesis, may have triggered auto-infarction, as indicated by necrotic changes like those reported by Minezaki et al (5).

Lastly, Kovacs et al described a case of spontaneous remission of hyperparathyroidism accompanied by disappearance of the adenoma on serial parathyroid scans (3). The authors highlighted 11 additional patients in the literature who exhibited clinical remission of primary hyperparathyroidism due to spontaneous infarction of the adenoma, supported by sufficient documentation and consistent clinical features. Ten of these patients experienced preceding symptoms consistent with hypercalcemia and/or prior documentation of hypercalcemia. Additional manifestations varied based on latency in diagnosis, alterations in serum calcium levels, and the location and degree of adenoma hemorrhage. The clinical scenarios associated with hemorrhage included three hypocalcemic crises, two hypercalcemic crises, one respiratory arrest secondary to a mediastinal hematoma, two patients with neck pain, and four patients with no symptoms apart from the premorbid symptoms of hypercalcemia, like our reported case. These cases emphasize the importance of long-term follow-up to assess for recurrence of hyperparathyroidism or, rarely, malignancy, considering the diverse clinical presentations, phasic laboratory values, and patient-specific factors involved.

4. Conclusion

In conclusion, these unique cases shed light on instances of parathyroid auto-infarction that, although rare, could spare patients from undergoing unnecessary surgical procedures. Parathyroidectomies are typically safe procedures with low morbidity and mortality rates, often resulting in short hospital stays and high success rates in curing hyperparathyroidism. Several instances of auto-infarction, as seen in this case and others, are important to acknowledge for pre-operative workup by both the surgeon and

referring provider. The cost versus benefit for non-surgical management in comparison to non-operative management with continued screening, including lab work and imaging, is important to consider while maintaining patient autonomy. By offering additional insights into clinical decision-making for this unique patient population, we aim to contribute as a valuable resource.

References

1. Pokhrel B, Leslie S, Levine S. *Primary hyperparathyroidism*. StatPearls, 2023. <https://www.ncbi.nlm.nih.gov/books/NBK441895/>
2. Kara E, Della Valle E, De Vincentis S, Rochira V, Madeo B. *Cured primary hyperparathyroidism after fine-needle aspiration biopsy-induced parathyroid disappearance*. Endocrinol Diabetes Metab Case Rep, 2017. pp17-0125. <https://pubmed.ncbi.nlm.nih.gov/29204278/>
3. Kovacs K.A, Gay J.D. *Remission of primary hyperparathyroidism due to spontaneous infarction of a parathyroid adenoma: Case report and review of the literature*. Medicine (Baltimore), 1998. 77(6):398-402.
4. Liu Y., Li J., Liu H., Yang H., Qiao J., Wei T., Wang T., Yu Y. *Spontaneous Remission After a Hypercalcemic Crisis Caused by an Intracystic Hemorrhage of Bilateral Parathyroid Adenomas: A Case Report and Literature Review*. Front Endocrinol, 2021. <https://pubmed.ncbi.nlm.nih.gov/34759892/>
5. Minezaki M., Takashi Y., Ochi K., Mitsuoka R., Yamao Y., Kudo T., Kawanami D., Kobayashi K., Abe I. *Reduction in parathyroid adenomas by cinacalcet therapy in patients with primary hyperparathyroidism*. J Bone Miner Metab, 2021. 39(4): pp.583-588. <https://pubmed.ncbi.nlm.nih.gov/33409573/>
6. Novodvorsky P., Hussein Z., Arshad M.F., Iqbal A., Fernando M., Munir A., Balasubramanian S.P. *Two cases of spontaneous remission of primary hyperparathyroidism due to auto-infarction: different management and their outcomes*. Endocrinol Diabetes Metab Case Rep, 2019. pp18-0136. <https://edm.bioscientifica.com/view/journals/edm/2019/1/EDM18-0136.xml>