Percutaneous Transsternal Cryoablation of Ectopic Parathyroid Adenoma in the Anterior Mediastinum

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Ectopic parathyroid adenomas are common in the context of hyperparathyroidism and represent a unique challenge in terms of localization and treatment. Often they are related to higher serum calcium levels than those associated with parathyroid adenomas in typical locations. Additionally, ectopic adenomas often lead to higher morbidity due to failed parathyroid exploration and multiple attempts at surgical removal. We present two cases of computed tomography–guided percutaneous transsternal cryoablation of ectopic parathyroid adenomas in the anterior mediastinum, one after failed surgical resection and the other after failed transarterial embolization. Cryoablation may represent a safe and effective alternative to surgery or embolization and should be included in the therapeutic algorithm in patients with percutaneously accessible lesions.

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Primary hyperparathyroidism is characterized by elevated parathyroid hormone (PTH) and calcium and associated with nonspecific symptoms like fatigue, muscle weakness, constipation, confusion, loss of appetite, and bone and joint pains. Parathyroid adenomas are responsible for 85% of the cases of primary hyperparathyroidism. In 10% to 36% of cases, the tumors are located ectopically [1, 2], with the most common ectopic locations being the mediastinum in close relation to the thymus (20%), the posterior mediastinum (5% to 10%), the thyroid gland (5%), and the carotid sheath (1%) [2]. The location of the hyperfunctioning gland is identified using a sestamibi scan with single-photon emission computed tomography (CT) with a sensitivity ranging from 82% to 100% [3, 4]. The accuracy of localization improves substantially with concurrent use of ultrasound [5]. Surgical resection is the current mainstay of treatment. Persistent hypercalcemia is observed in 10% to 15% of neck exploration surgeries [6]. We describe two patients treated with percutaneous cryoablation of parathyroid adenomas in the anterior mediastinum, one after failed treatment with parathyroidectomy and the other after unsuccessful arterial embolization.

1. Case Presentation

A. Case 1

A 38-year-old woman presented to an outside hospital with fatigue, myalgia, change in bowel habits, arthritis, chest pain, increased blood pressure, anxiety, sweating episodes, bone pain, and weight loss. Her parathyroid hormone levels were elevated, with a calcium level of 11.5 mg/dL. She was referred to our institution for further evaluation and treatment.

Abbreviations: CT, computed tomography; PTH, parathyroid hormone.
and nephrolithiasis. She was found to have elevated serum calcium and PTH. Parathyroidectomy temporarily resolved her symptoms. When the symptoms returned 1 month later, further investigation at our institution showed PTH of 356.4 pg/mL (normal range: 12 to 88 pg/mL) and calcium of 11.8 mg/dL (normal range: 8.6 to 10.2 mg/dL). Parathyroid scintigraphy demonstrated residual parathyroid activity in the anterior mediastinum (Fig. 1A). Chest CT demonstrated a 10-mm × 15-mm enhancing nodule in the anterior mediastinum (Fig. 1B). Surgical resection would have required median sternotomy. The patient chose to undergo CT-guided cryoablation. Two hours before ablation, PTH was 436.1 pg/mL and calcium was 11.4 mg/dL. She was administered general anesthesia and intubated for the duration of the procedure. The first cryoablation probe (Galil Medical Inc., Arden Hills, MN) was introduced through the sterno-clavicular joint, directed toward the superior aspect of the lesion.

**Figure 1.** (A) Parathyroid scintigraphy reveals a focus of increased radiotracer accumulation in the anterior mediastinum. (B) Chest CT demonstrates a 10-mm × 15-mm enhancing nodule in the anterior mediastinum. (C) Intraprocedural image depicts the second probe, which was introduced through an introducer needle in a transsternal fashion and directed toward the inferior aspect of the lesion.
lesion. The second probe was introduced in a transsternal fashion through an 11-gauge bone biopsy needle introducer, directed toward the inferior aspect of the lesion (Fig. 1C). Three freeze-thaw cycles were used to achieve complete tissue necrosis. CT showed ice ball formation within the location of the lesion. One-hour postablation intact PTH was 212.1 pg/mL (51.4% decrease) and calcium was 11.4 mg/dL. Ninety-minute postablation intact PTH was 254.0 pg/mL and calcium was 11.4 mg/dL, and 3-hour postablation intact PTH was 195.7 pg/mL and calcium was 11.7 mg/dL. One-year follow-up showed calcium of 9.6 mg/dL and PTH of 74.4 pg/mL. Nuclear medicine scan revealed no recurrent/residual tumor within the thyroid bed or mediastinum. Her symptoms had improved substantially.

B. Case 2

A 70-year-old man presented with severe diffuse muscle aches, joint pains, and bone pain. Laboratory work revealed that PTH was 167.3 pg/mL and calcium was 10.8 mg/dL. Chest CT revealed an “S”-shaped enhancing mass in the anterior mediastinum behind the sternum and slightly left of midline (Fig. 2A). Parathyroid scintigraphy identified a focus of increased activity in the anterior mediastinum representing an ectopic parathyroid adenoma (Fig. 2B). Surgery would have required a sternotomy, and the patient declined this option. In an attempt at less invasive treatment, he underwent selective transcatheter ethanol embolization of branches of the left internal mammary artery. Intact PTH the next day was 110 pg/mL and calcium was 10.7 mg/dL. Intact PTH and calcium continued to be elevated at 1- and 2-month follow-up, and his symptoms failed to improve. Postprocedural CT showed deposition of alcohol only in the inferior portion of the adenoma with sparing of the superior portion. No other obvious feeding vessels could be identified on CT angiography so repeat embolization was not expected to be beneficial. Percutaneous, CT-guided cryoablation was performed. Two hours before ablation, intact PTH was 239.4 pg/mL and calcium was 10.5 mg/dL. He was administered general anesthesia and intubated for the duration of the procedure. Eleven-gauge bone biopsy needles introduced transsternally provided access to the mass (Fig. 2C). Two cryoablation probes (Galil Medical Inc.) were inserted through the bone biopsy needles.

Figure 2. (A) Chest CT reveals an “S”-shaped enhancing mass in the anterior mediastinum. (B) Parathyroid scintigraphy detects a focus of increased activity in the anterior mediastinum. (C) Intraprocedural image depicts the 11-gauge bone biopsy needles introduced transsternally and percutaneously guided by CT.
The first was extended diagonally within the lesion. The second was oriented perpendicularly through the superior aspect of the lesion. Two freeze-thaw cycles were used. CT verified appropriate ice ball positioning in the retrosternal space. One-hour postablation intact PTH was 174.9 pg/mL (26.9% decrease) and calcium was 10.1 mg/dL. Two-hour postablation intact PTH was 207.8 pg/mL and calcium was 10.2 mg/dL. One-day postablation intact PTH was 96.1 pg/mL and calcium was 10.9 mg/dL. Two-month follow-up revealed PTH of 44.2 pg/mL and calcium of 10 mg/dL with resolution of symptoms.

2. Discussion

Hyperparathyroidism involves symptoms related to hypercalcemia and bone resorption, such as bone pain, arthritis, anorexia, weight loss, constipation, abdominal pain, impaired memory, confusion, fatigue, muscle weakness, and itching [7, 8]. Workup includes a total serum calcium level, ionized calcium level, phosphate level, intact PTH level, and 24-hour urine calcium level. A sestamibi scan is performed to locate the gland. Most parathyroid adenomas (92.7%) have increased radiotracer uptake on immediate images and increased retention on delayed images [9]. Four-gland exploration is considered the “gold standard” for patients undergoing parathyroidectomy; however, many centers opt for a minimally invasive directed parathyroidectomy [10]. The potential complications of parathyroidectomy include infection, bleeding, recurrent laryngeal nerve injury, superior laryngeal nerve injury, hypocalcemia, and persistent disease due to ectopic glands not found during surgery [11]. The risk of complications increases for repeat surgical exploration [12]. Ectopic parathyroid adenomas are found in 2.3% of patients undergoing neck exploration [13]. The most common ectopic location of parathyroid glands is the anterior mediastinum, accounting for 1.3% of cases with parathyroid adenomas [13]. Mediastinal adenomas are excised through sternotomy, lateral thoracotomy, or video-assisted mediastinal/thoracoscopic surgery, which are associated with up to 21% risk of morbidity [12]. Ectopic adenomas can also be treated using transcatheter embolization with alcohol with success rates of 63% to 83% [13–15]. Possible complications from this procedure include chest pain, bradycardia, respiratory distress, hoarseness of voice, hiccups, and acute thyroiditis [13].

Cryoablation involves freezing tissue at temperatures between −20°C and −60°C, followed by rapid thawing, resulting in cell membrane disruption and cell death. To destroy tumor tissue adequately, the entire target volume must be subjected to cytotoxic temperatures, which can necessitate the use of multiple cryoprobes [11]. Percutaneous cryoablation is an accepted mode of treatment of small renal masses in patients not suitable for surgery or who require nephron preservation, with reported overall survival of 78% to 97.8%, cancer-specific survival of 98% to 100%, and disease-free survival of 80% to 97%. Cryoablation is a particularly useful modality in the mediastinum because of the ability to see the ice ball ablation zone and the relative safety of delicate structures nearby [16].

Smirniotopoulos et al. [12] report a similar case in which a patient with persistently elevated PTH and calcium and who previously underwent surgical parathyroidectomy had a mediastinal ectopic adenoma identified on imaging. Due to the increased risk of repeat surgical intervention, the patient underwent percutaneous cryoablation. They also used a transternal approach using a bone biopsy needle and successfully treated the lesion. That case and ours describe an important minimally invasive option for the treatment of mediastinal ectopic parathyroid adenomas, where the other options for treatment involve a repeat surgery with increased risk of morbidity and highly invasive sternotomy or thoracotomy for access to the retrosternal nodule [12]. Mediastinal cryoablation is indicated when the lesion can be accessed percutaneously with or without the use of a bone biopsy needle to create a path through the sternum and contraindicated if the patient is unable to undergo anesthesia, is coagulopathic, has a history of mediastinal infections, or has a history of cancer in the sternum. Anatomic considerations, such as history of coronary artery bypass graft surgery with involvement of the internal mammary artery, are important when performing percutaneous procedures in the chest. Risks of percutaneous cryoablation in the anterior
mediastinum include bleeding, puncturing the heart and great vessels, pneumothorax, and nerve injury [17]. Our patients did not have any complications.

Measurement of intraoperative PTH is useful for ensuring successful removal of the target tissue during parathyroidectomy because of the hormone’s short 2- to 4-minute half-life [5, 12]. A decline of >50% 10 minutes following gland removal is reassuring for cure [5]. The previous parathyroid cryoablation case study reported a big spike in intact PTH 10 minutes post ablation, perhaps due to hormone release during tissue necrosis [12]. They reported a reduction in PTH 1 hour post ablation [12]. We also found that both of our patients had a decrease in postablation intact PTH after 1 hour. Subsequent PTH monitoring revealed a transient increase at 1.5 to 2 hours and eventual downtrend. Cryoablation involves two to three freeze-thaw cycles, with the first thaw being a complete 5 minutes and the last thaw typically lasting only long enough to remove the cryoprobe from the tissue, which remains partially frozen, theoretically to provide analgesic effects. The transient increase in intact PTH that we saw could have been due to additional stored hormone release as the tissue slowly thawed. Because we did not measure PTH at 10 minutes, we did not see the same initial large spike in PTH as the other study [12]. The combination of trending intact PTH postprocedurally and visualization of ice ball formation on CT contribute to the determination of successful treatment of the adenoma.

In summary, ectopic parathyroid adenomas present a unique challenge in the setting of symptomatic hyperparathyroidism in terms of locating and treating the lesion. Oftentimes, the ectopic adenoma is not resected during the first parathyroidectomy and hyperparathyroidism persists, necessitating further treatment. When the adenoma is located in the mediastinum, typical surgical approaches involve sternotomy, thoracotomy, and video-assisted mediastinal/thoracoscopic surgery. Transcatheter embolization has also been used with varying success. This study suggests that CT-guided percutaneous transsternal cryoablation may represent a safe alternative to surgery or embolization and should be considered as part of the therapeutic algorithm for percutaneously accessible lesions.

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