Regression of Calcinosis following Treatment with Radiofrequency Thermoablation for Severe Secondary Hyperparathyroidism in a Hemodialysis Patient

Rending Wang¹, Tianan Jiang², Zhimin Chen¹ and Jianghua Chen¹

Abstract

We herein present the case of a 41-year-old man who was misdiagnosed with a recurrent right shoulder tumor and underwent surgery twice. The pathological diagnosis was calcinosis. Secondary hyperparathyroidism was confirmed on further examination and the patient was therefore treated with two sessions of percutaneous ultrasonographically-guided radiofrequency tissue ablation. During the 20-month follow-up, the patient underwent four-hour hemodialysis three times a week. The calcinosis nearly completely resolved, and the PTH level was mildly elevated without the administration of any further medical therapy. Percutaneous ultrasonographically-guided radiofrequency tissue ablation is a feasible, safe and effective nonsurgical alternative treatment for secondary hyperparathyroidism.

Key words: secondary hyperparathyroidism, calcinosis, radiofrequency thermoablation

(DOI: 10.2169/internalmedicine.52.8454)

Introduction

The development of secondary hyperparathyroidism during dialysis is one of the main problems that occur in the management of chronic renal failure patients and it may lead to calcinosis (1, 2). Although progress has been made in medical therapy (oral active vitamin D sterols, phosphate binders and intermittent high doses of calcitriol) (3, 4), performing parathyroidectomy is mandatory for preventing chronic hypercalcemia, bone resorption and calcinosis, especially in patients with marked parathyroid hyperplasia in whom metabolic disorders are refractory to a medical approach (1, 5).

Parathyroidectomy is a treatment for symptomatic primary hyperparathyroidism and secondary hyperparathyroidism resistant to medical therapy. A minimally invasive alternative is needed, especially for patients with high surgical and anesthetic risks. Over the last few years, different percutaneous ablation modalities have been developed, such as ethanol injection (2, 6-12), acetic acid injection (13), calcitriol injection (14), laser ablation (15) and radiofrequency thermoablation (RFA) (16). RFA is an interesting and new alternative therapeutic option for the treatment of hyperparathyroidism, in particular, for nonsurgical patients with unacceptable risks of postoperative morbidity or those who have previously undergone surgery of the neck. Additionally, in cases of recurrence, RFA allows for the complete destruction of hyperfunctioning parathyroid tissue. The RFA procedure definitively resolves pathologic conditions without the need for chronic daily medication (17). Good results for RFA at different levels, and especially in patients with primary or metastatic liver tumors, have been reported (18). Ultrasound-guided hyperparathyroidism treatment with radiofrequency is at present experimental, and only a few cases have so far been reported in animals (19) and humans (16, 20). We herein present the case of a patient with secondary hyperparathyroidism who showed recurrent right juxta-articular calcinosis of the shoulder and underwent surgery twice. The pathological diagnosis was confirmed to be calcinosis. The patient received RFA and his clinical symptoms remarkably resolved within a 20-month follow-up period.

¹Kidney Disease Center, The First Affiliated Hospital, Medical College of Zhejiang University, China and ²Ultrasonic Department, The First Affiliated Hospital, Medical College of Zhejiang University, China

Received for publication June 29, 2012; Accepted for publication August 16, 2012
Correspondence to Dr. Jianghua Chen, chenjianghua@zju.edu.cn
Case Report

A 41-year-old man with chronic renal failure had been on hemodialysis for nine years and had suffered from recurrent swelling of the right shoulder for six years. Nine years previously, the patient underwent regular hemodialysis due to uremia without any significant clinical signs. Six years previously, he complained of right shoulder swelling and pain with easy fatigability. At that time, the serum phosphate level was elevated to 2.85 mmol/L, the calcium level was normal at 2.54 mmol/L and the PTH level was 1,256 pg/mL. Four years previously, following an enlargement of the shoulder tumor (22 × 22 cm in size), he was admitted to our bone department. MRI showed the presence of a tumor in the right shoulder, and the patient underwent surgery. Further examinations revealed white, soybean-curd-like residue, and histology showed calcium deposition (Fig. 1) in December, 2006.

After surgery, the tumor decreased in size. However, one year later, the patient underwent a second operation due to enlargement of the shoulder tumor. His shoulder remained enlarged and he was admitted to our clinic with elevated levels of parathyroid hormone (PTH), serum calcium, serum phosphorus and serum creatinine (greater than 2,500 pg/mL, 2.19 mmol/L, 2.98 mmol/L and 1,165 μmol/L, respectively) along with right shoulder ectopic tissue calcification (Fig. 2A). Other clinical parameters such as routine blood markers, tumor markers (AFP, CEA, CA199, CA125) and coagulation factors were all normal. An ultrasound examination detected two hypoechoic enlarged inferior parathyroid glands (at the right inferior pole of the thyroid gland measuring 1.5 × 1.1 cm in size and at the left inferior pole of the thyroid gland measuring 1.6 × 1.1 cm in size, Fig. 3A, 3B) suggestive of nodular hyperplasia, an advanced type of parathyroid hyperplasia. Hyperfunction was confirmed on 99mTcMIBI scintigraphy. A diagnosis of secondary hyperparathyroidism was made.

The patient received active vitamin D sterols (Rocaliro®) at a dose of 2.5 μg twice a week with pulse treatment for one month. The PTH level remained higher than 2,500 pg/mL and a diagnosis of adenoma-like hyperplasia resistant to medical drug therapy was considered. In cases such as this, written informed consent is obtained from these patients, who are of course free to choose their treatment and decide whether they prefer alternative continued chronic medical treatment, minimally invasive procedures or traditional surgery. The patient strongly requested minimally invasive procedures. The use of ultrasound-guided RFA was selected. In July, 2010, after the administration of conscious sedation and local anesthesia, the procedure was performed using a 1 cm bipolar needle with two linear electrodes at the tip of the applicator (RFITT Celon AG Medical Instruments Teltow/ Berlin, Germany). Radiofrequency heat was applied until changes in the entire right inferior parenchyma of the mass were apparent on sonography with color Doppler function. The patient was monitored for any adverse effects. The serum total and ionized calcium, phosphorus and PTH concentrations were monitored the day after RFA, and the laryngeal function was assessed and cervical ultrasonography was performed. Preoperative and postoperative laryngeal examinations were conducted with videoendoscopy by an external otolaryngologist. After confirming that no injury had occurred to the nerve, the hypoechoic enlarged left inferior parathyroid gland was treated with RFA three days after the first RFA (in July, 2010). Any complications that arose were observed at the end of treatment. The patient’s recovery was uneventful.
The patient received regular follow-up, and no additional doses of active vitamin D sterols or phosphate binder were given. Right shoulder X-rays and the levels of serum calcium, phosphorus and PTH were examined regularly. X-ray of the right shoulder showed decreases in ectopic tissue calcification (Fig. 2A, B, C, D). Normal levels of serum calcium and phosphorus and mild PTH elevation were observed after therapy. The concentration of calcium-phosphorus products was reduced from 6.53 mmol/L^2 (59.4 mg/dL^2) before RFA therapy to 4.09 mmol/L^2 (50.7 mg/dL^2) one month after RFA therapy and 2.31 mmol/L^2 (28.6 mg/dL^2) 20 months after RFA therapy (Table).

### Discussion

The RFA procedure was first described in the early 1990s. It is a minimally invasive ablation technique based on induction of thermal injury to tissue through the deposition of electromagnetic energy. The transmission of alternating electrical current created by the RFA generator occurs through special needle electrodes placed percutaneously inside lesions. The electrical current causes ionic agitation that results in the development of frictional heat around the electrode and the creation of areas of coagulative necrosis. For the last several years, RFA has been used to treat primary and metastatic liver tumors, particularly “unresectable” liver tumors (21-23). In addition, the use of RFA has also been expanded to other organs. RFA is becoming one of the standard therapies for treating tumors of the kidneys and bone under appropriate indications. Other sites for which RFA has been used for tumor ablation that are considered to be experimental or investigational include the prostate, lungs, pancreas, osteoid osteomas, islet cells, breasts, endocrine organs such as the adrenal glands, head and neck organs, retroperitoneal organs, pelvic organs, subcutaneous or muscular tissues and so forth (24-26).

Hyperparathyroidism has traditionally been treated with open surgery using cervical transverse incisions. Currently, the standard treatment for hyperparathyroidism secondary to parathyroid adenoma or hyperplasia is surgical resection. Parathyroidectomy can presently be performed safely and effectively, although it is invasive. Minimally invasive parathyroidectomy using smaller incisions has been recently performed, and other methods, such as ethanol injection are also used in clinical therapy (11, 12). A recent observational study reported by Koiwa et al (11) showed that superior efficacy is obtained with percutaneous ethanol therapy (PEIT) when the treatment is restricted to patients with no more than one hyperplastic gland ≥0.5 mm^3. The author reported that, when multiple hyperplastic parathyroid glands are present, PEIT is somewhat ineffective, necessitating the use of increased numbers of injections. The incidence of injection-related complications associated with PEIT, including hemorrhage, recurrent laryngeal nerve palsy caused by ethanol leakage and adhesion to surrounding tissue, increases as the number of injections increases. Therefore, the Japanese PEIT guidelines indicate that long-term therapeutic effects may be unsatisfactory in patients with multiple hyperplastic glands, in particular, in those in whom the number of glands is three or more, as the risk of complications increases with the number of injections (27).

Percutaneous RFA for the parathyroid is the least invasive parathyroid therapy and it requires almost no incisions. Carrafiello and associates (16) reported a case of secondary hyperparathyroidism that was successfully treated with ultrasonographically-guided percutaneous radiofrequency ablation. The effectiveness of this treatment should be assessed in both the short and long terms. In contrast to RFA for “unresectable malignant” tumors of the liver, RFA for hyperparathyroidism is generally used to treat “resectable benign” lesions; therefore, absolute safety can thus be achieved. Burn injury to surrounding organs, including the esophagus, trachea, vascular structures and recurrent nerve, is a major concern with RFA. To avoid thermal injury to these structures, refining the RFA technique and instrumentation is necessary. First, with respect to intraoperative assessment, real-time sonography of the parathyroid glands or

### Table. The Levels of PTH, Serum Calcium and Phosphorus before and after RFA Treatment

<table>
<thead>
<tr>
<th>Time after RFA(months)</th>
<th>0</th>
<th>1</th>
<th>6</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTH level (pg/mL)</td>
<td>&gt;2,500</td>
<td>505</td>
<td>485</td>
<td>402</td>
</tr>
<tr>
<td>Serum calcium(mmol/L)</td>
<td>2.19</td>
<td>1.52</td>
<td>1.82</td>
<td>1.64</td>
</tr>
<tr>
<td>Serum phosphorus (mmol/L)</td>
<td>2.98</td>
<td>2.69</td>
<td>1.45</td>
<td>1.41</td>
</tr>
</tbody>
</table>

Figure 3. An ultrasonic examination of bilateral parathyroid enlargement. A: Right side of the neck, B: Left side of the neck.
contrast-enhanced color Doppler imaging and intraoperative intact parathyroid hormone monitoring allow for quick reliable assessment of parathyroid gland hormone secretion during parathyroidectomy (28). Second, lidocaine or normal saline should be injected into the area around the adenoma or hyperplasia and can be used as a heat insulator to isolate the nerve. Third, patients with bilateral hyperplasia should undergo RFA of one side during the first operation and RFA of the other side a few days later. Through this method, the doctor can avoid the occurrence of bilateral recurrent nerve injury.

The development of secondary hyperparathyroidism during dialysis is one of the main problems that occurs in the management of chronic renal failure patients (2). Calcification has been described to occur in patients with chronic renal failure, along with high levels of calcium-phosphorus products and progressive secondary hyperparathyroidism (1). Treating calcification is challenging and therapy should target the main precipitating factors, most notably, secondary hyperparathyroidism and calcium-phosphate product elevation. Although vascular calcification is stabilized or improved with nocturnal hemodialysis, patients with very high levels of PTH at baseline (>1,000 ng/mL) do not show significant improvements in parathyroid hormone status (29). Several case reports have indicated that secondary hyperparathyroidism and calcinosis can be completely or remarkably improved with parathyroidectomy (30-32). Our patient’s case is a dramatic example of near complete resorption of soft tissue juxta-articular calcification of the shoulder in secondary hyperparathyroidism after treatment with RFA. This improvement can be attributed to significant decreases in the levels of PTH and calcium-phosphorus products.

Carrafiello and associates (16) reported safety and effectiveness in three patients in whom the longest follow-up was seven months. In our case, we found that near complete resolution of calcinosis was achieved during a 20-month follow-up period. Although hyperplasia was not detected in the two remaining glands, the mild PTH elevation observed in our patient may have been caused by persistent hyperparathyroidism persisting after two rounds of RFA therapy, thus indicating that a longer time is required to evaluate the effectiveness of RFA therapy for hyperparathyroidism. Currently, our patient is doing well after undergoing RFA, and the follow-up time in this case is the longest reported in the literature. What is the exact indication for RFA? Machi (33) reported that hyperparathyroidism caused by four-gland hyperplasia is not a good indication for RFA, although single-gland adenoma may be an appropriate indication for RFA treatment. Postsurgical recurrent hyperparathyroidism may also be a good indication due to the difficulty of reoperation. However, treatment of the parathyroid gland at unusual or ectopic locations should be considered for RFA, as suggested by Machi. It is unlikely that ectopic parathyroid hyperplasia is a good indication for RFA, as it seems very difficult to target ectopic glands, particularly those in the mediastinum. In our opinion, single-gland adenoma or hyperplasia and postsurgical recurrent hyperparathyroidism are indications for RFA treatment, and more than one unilateral or bilateral gland adenoma or hyperplasia can be considered for fractionated RFA. RFA may cause surrounding tissue fibrosis, and the incidence of RFA-related complications, including hemorrhage and recurrent laryngeal nerve palsy, increases as the number of RFA treatments increases. If gland hyperplasia is recurrent, then the difficulty of performing such surgery may increase. The decision regarding whether to perform RFA or surgery first is an important clinical problem. Therefore, to further evaluate the effectiveness of RFA for treating hyperparathyroidism, conducting randomized, controlled protocol trials of RFA and providing long-term follow-up after RFA treatment are essential.

The authors state that they have no Conflict of Interest (COI).

References