Percutaneous ultrasonographically guided radiofrequency heat ablation for treatment of primary hyperparathyroidism in dogs

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Objective—To evaluate the efficacy and safety of ultrasonographically guided radiofrequency heat ablation of parathyroid masses in dogs with primary hyperparathyroidism.

Design—Clinical trial.

Animals—11 dogs.

Procedure—In all dogs, either 1 or 2 parathyroid masses were evident ultrasonographically. Dogs were anesthetized, and a 20-gauge over-the-needle catheter was directed into the parathyroid mass via ultrasonographic guidance. Radiofrequency heat was applied to the stylet of the catheter until there was sonographically apparent change to the entire parenchyma of the mass. Serum total and ionized calcium and parathyroid hormone concentrations were monitored daily for 5 days after the ablation procedure and again at 1, 2, and 3-month intervals, if possible. Dogs were monitored for adverse effects.

Results—One treatment was required in 6 dogs, 2 treatments were required in 2 dogs, and treatment was unsuccessful in 3 dogs. Serum total and ionized calcium concentrations were within reference ranges within 2 days of the last procedure in all 8 successfully treated dogs. Serum parathyroid hormone concentration was decreased 24 hours after treatment in all 8 dogs. Hypocalcemia developed in 5 of the 8 successfully treated dogs, all of which required treatment. One dog had a transient voice change. Other adverse effects were not reported.

Conclusions and Clinical Relevance—Ultrasonographically guided radiofrequency heat ablation of parathyroid masses is a safe and effective alternative to surgery in dogs with primary hyperparathyroidism. (*J Am Vet Med Assoc* 2001;218:1106–1110)

Primary hyperparathyroidism (PHP) is a recognized cause of hypercalcemia in dogs. The most common cause of PHP is a functional adenoma of the parathyroid chief cells. Parathyroid adenocarcinomas or autonomously secreting hyperplastic parathyroid glands are less common.[1-3] Dogs with PHP are hypercalcemic because of excessive autonomous secretion of **parathyroid hormone (PTH)**.[1-3] Most parathyroid masses can be viewed by use of cervical ultrasonography, whereas normal parathyroid tissue is difficult to view, even with a high-resolution transducer.[4,5] Abnormal parathyroid tissue typically appears as a solitary hypoechoic mass in close proximity to the thyroid lobe.[6,7] Conventional treatment for dogs with PHP is excision of the abnormal tissue.[3]

Intralesional ultrasonographically guided ethanol injection has been used in humans and dogs as an alternative to surgery for the treatment of primary hyperparathyroidism.[8-13] Recently, ultrasonographically guided radiofrequency heat ablation has been used as an alternative to chemical ablation for treatment of small hepatic masses in humans.[14,15] Heat ablation may cause fewer adverse effects than ethanol ablation. To our knowledge, no studies evaluating radiofrequency heat ablation of parathyroid masses have been performed in either humans or dogs. The purpose of the study reported here was to evaluate the efficacy of ultrasonographically guided radiofrequency heat ablation of parathyroid masses in dogs with PHP.

Materials and Methods

Dogs—Dogs brought to the University of California Davis **Veterinary Medical Teaching Hospital (VMTH)** for evaluation and treatment of hypercalcemia caused by PHP were eligible for inclusion in the study. Dogs were included if they met the following criteria: clinical signs consistent with hypercalcemia (ie, polyuria, polydipsia, muscle weakness), persistently increased serum total and ionized calcium concentrations (at least 3 separate tests during a period of > 30 days' duration), serum phosphorus concentration within or below reference limits, serum PTH concentration within or above reference limits, no detectable serum PTH-related-protein,[a] and no evidence of concurrent disease that could result in hypercalcemia (specifically, no evidence of renal dysfunction or neoplasia). In addition, dogs were required to have 1 or 2 ultrasonographically apparent hypoechoic masses in or near the thyroid gland with features that were consistent with descriptions of parathyroid adenomas.[6] A 10-MHz linear phased-array transducer and standard ultrasonography machine were used.[b] Informed owner consent was obtained.

A thorough history was obtained, and a physical examination, CBC, serum biochemical analyses, urinalysis, thoracic radiography, and abdominal ultrasonography were performed on dogs prior to inclusion in the study. Dogs that had any abnormalities other than those attributed to untreated PHP and dogs that had received any medication that could alter serum calcium or PTH concentrations during the 3-month period preceding treatment were excluded from the study. For dogs included in the study, ultrasonographic size measurements of the parathyroid masses' length, width, and height were recorded for comparisons after heat ablation.

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Serum total and ionized calcium, phosphorous, and PTH concentrations were assayed immediately before treatment.

Heat ablation procedure—Dogs were anesthetized by IV administration of propofol or inhalation of isoflurane and positioned in dorsal recumbency with the neck extended. The ventral cervical region was clipped and aseptically prepared. A small area on the ventral portion of the abdomen was clipped, and the dog was grounded by use of a disposable cautery ground pad. A 20-gauge over-the-needle IV catheter[c] was used after the plastic hub had been removed. Sterile gel was applied to the ventral cervical region, and the parathyroid mass was identified ultrasonographically. With ultrasonographic guidance, the catheter with stylet was then guided into the parathyroid mass. The catheter sleeve acted as an insulator for the surrounding normal soft tissues. An insulated wire connection was made between the radiofrequency unit[d] and catheter stylet. The radiofrequency unit was equipped with a ballast resistor to compensate for the high impedance of the needle. Radiofrequency energy was applied at 10 to 20 W for 30 to 90 seconds until sonographically apparent tissue change was subjectively viewed (**Fig 1**). More specifically, the machine was set at 10 W for the first 10 to 20 seconds. If echogenic bubbles were not sonographically viewed at the needle tip at this time, the wattage was increased by increments of 5 every 10 seconds until echogenic foci became apparent within the tissue. If an audible popping sound could be heard, the maximum heat application had been reached and additional increases in the machine settings were not made.

The needle was arbitrarily redirected multiple times, if necessary, in an attempt to ablate the entire mass. If 2 ipsilateral masses were identified, ablation of both masses was performed during the same anesthetic procedure. However, if masses were identified on contralateral sides, 1 mass was heat ablated, and the contralateral mass was ablated no sooner than 10 days later. Dogs were allowed to recover from anesthesia immediately after the procedure.

Monitoring—After treatment, serum ionized calcium and PTH concentrations were measured daily for 5 days, weekly for 1 month, and monthly thereafter. Physical examinations were performed every 12 hours for the first 5 days to determine whether there were signs of hypocalcemia, signs of pain or swelling at the treatment site, voice change, or respiratory distress. Arbitrary criteria were chosen to diagnose clinically important hypocalcemia. If, at any time, dogs developed signs of hypocalcemia or if serum ionized calcium concentration decreased to < 0.9 mEq/L, supplementation with vitamin D and calcium was instituted, using a standard treatment approach.[3] Repeat ultrasonography of the cervical region was performed on dogs that returned to the VMTH for follow-up.

When evaluated, serum total calcium concentration was determined by use of colorometric evaluation.[e] Ionized calcium concentration was determined by use of ion-selective electrode analysis.[f] Serum PTH concentration was determined by use of a validated 2-site immunoradiometric method that recognizes amino- and carboxy-terminal ends of the intact molecule.[16]

Results

Eleven dogs examined between September 1999 and June 2000 were included in the study. Dogs were between 6 and 12 years old and included multiple breeds.

Prior to treatment, serum total calcium concentrations ranged from 13.0 to 15.2 mg/dl (mean ± SD, 14.0 ± 1.2 mg/dl; reference range, 9.4 to 11.6 mg/dl), serum ionized calcium concentration ranged from 1.62 to 2.07 mEq/L (mean, 1.9 ± 0.6 mEq/L; reference range, 1.12 to 1.35 mEq/L), serum phosphorus concentrations ranged from 1.5 to 3.4 mg/dl (mean, 2.4 ± 0.7 mg/dl; reference range, 2.5 to 6.2 mg/dl), and serum PTH concentrations ranged from 6.0 to 27.2 pmol/L (mean, 19.7 ± 18.9 pmol/L; reference range, 2 to 13 pmol/L). Serum PTH-related protein was undetectable in all dogs.

A solitary parathyroid nodule was identified by use of cervical ultrasonography on the left side of the neck in 7 dogs. Four dogs had 2 nodules each. Three of these 4 dogs had both nodules on the left side of the neck, and 1 dog had 1 nodule associated with each thyroid lobe. The ultrasonographic appearance of the 15 masses was similar. All masses were spherical or ovoid and hypoechoic to the surrounding thyroid parenchyma. Length varied from 0.3 to 1.1 cm.

Anesthesia time varied from 20 to 60 minutes. Most of the anesthesia time was spent ensuring appropriate needle placement. As our experience increased, anesthesia time decreased. The needle was redirected, and heat was applied 3 to 4 times in each dog until the entire mass appeared to have been treated. After treatment, the sonographic appearance of the gland became hyperechoic in comparison to the pretreatment appearance. Echogenic bubbles that formed in the heated tissue could be seen at the needle tip.

Seven of the 11 dogs responded to the initial treatment. Six of these 7 dogs had unilateral masses, whereas 1 dog had contralateral masses; this dog underwent 2 heat ablation procedures at the preplanned 10-day interval. Serum total and ionized calcium concentration decreased to within the reference range within 5 days of heat ablation in these 7 dogs.

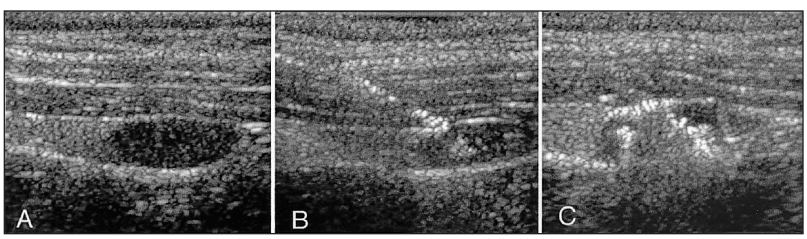

Figure 1—Left lateral sonographic images of an oval hypoechoic parathyroid nodule in a dog prior to heat ablation (A), with the insulated needle passing through the superficial soft tissues into the cranial aspect of the mass (B), and after heat ablation (C). Notice the hyperechoic foci within the parenchyma of the gland in image C.

Serum PTH concentration decreased to within or below the reference range within 24 hours of heat ablation in these dogs.

Serum ionized and total calcium concentration did not decrease within 5 days of heat ablation in 1 dog. This dog was retreated with heat ablation on day 5. Serum ionized and total calcium concentration decreased to reference range within 2 days after the second procedure. Serum PTH concentration also decreased to within the reference range during the first 24 hours after the second ablation procedure.

One dog had an initial response to treatment, which was characterized by serum ionized and total calcium concentration that decreased to reference range by day 5 and serum PTH concentration that decreased to reference range by day 1 after ablation. This dog was examined at day 30 for an unrelated surgical emergency. At that time, serum total calcium concentration was 14.0 mg/dl, and ionized calcium concentration was 1.45 mEq/L. Rather than repeating heat ablation, the parathyroid mass was removed during the emergency procedure. In the remaining 2 dogs, the parathyroid nodule repeatedly slid away from the needle tip. Heat ablation was never administered, and surgical removal of a parathyroid adenoma was performed in each dog. Therefore, 8 of 11 dogs were successfully treated with heat ablation (**Fig 2**).

Biochemical evidence of hypocalcemia, clinical tetany, or both was detected in 5 of the 8 dogs that had successful response to heat ablation (**Fig 3**). These 5 dogs all received vitamin D[g] and oral supplementation with calcium.[h] For 1 dog, supplementation was tapered off during a 6-month period and serum PTH concentration and serum total and ionized calcium concentrations were within reference limits 3 months after treatment was discontinued. Four dogs remain on tapering doses of vitamin D supplementation 1 to 9 months after ablation. Three dogs did not require vitamin D supplementation (**Fig 4**). Each of these 3 dogs had serum total and ionized calcium concentrations within reference ranges 3 to 8 months after ablation. One dog with a unilateral parathyroid mass developed a transient voice change immediately after heat ablation, which resolved within 5 days. It is uncertain whether the voice change developed secondary to intubation or the ablation procedure. Signs of pain, swelling, or respiratory distress were not detected in any of the dogs.

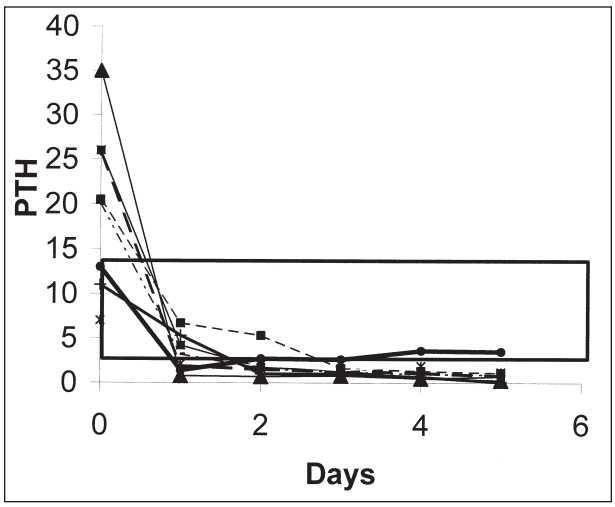

Figure 2—Serum parathyroid hormone (PTH) concentration (pmol/L; individual data points) of 8 dogs that were successfully treated for primary hyperparathyroidism. The reference range is outlined.

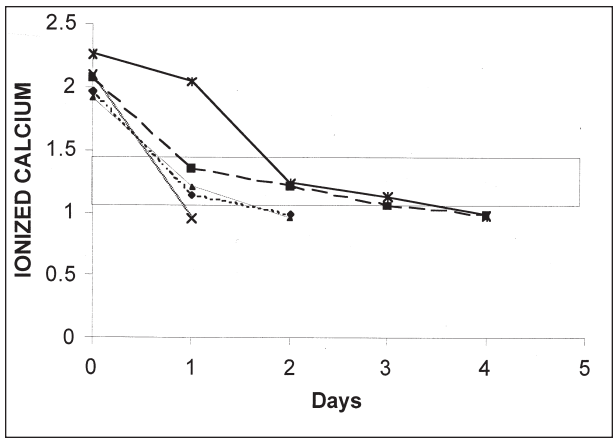

Figure 3—Serum ionized calcium concentrations (mg/dl; individual data points) in 5 dogs that were successfully treated for primary hyperparathyroidism on day 0 and eventually required vitamin D supplementation 1 to 4 days after treatment. The reference range is outlined.

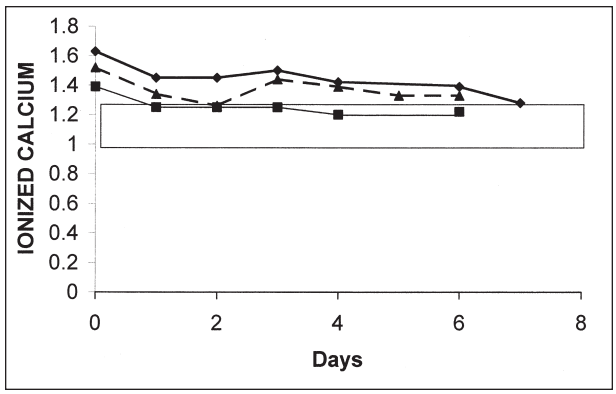

Figure 4—Serum ionized calcium concentrations (mg/dl; individual data points) in 3 dogs that were successfully treated for primary hyperparathyroidism on day 0 and did not require vitamin D supplementation. The reference range is outlined.

Discussion

Ultrasonography of the cervical region has become a valuable diagnostic tool. In healthy dogs, the thyroid glands can be easily identified, but parathyroid tissue is difficult to image.[4,5] If normal parathyroid tissue is viewed, it is hypoechoic in relation to adjacent thyroid tissue, located at either the cranial pole or midbody of the thyroid gland, and usually is < 0.2 cm in any dimension.[4,5] Abnormal parathyroid tissue usually appears as a solitary round-to-oval hypoechoic mass closely associated with a thyroid lobe. In general, hyperplastic glands are < 0.4 cm in any dimension, and parathyroid adenomas or adenocarcinomas are > 0.4 cm.[6,7] Although less common, 2 discrete masses causing PHP have been reported.[1]

Ultrasonographically guided chemical ablation using ethanol has been used for the treatment of PHP in humans.[8-12] Ethanol causes coagulation necrosis and vascular thrombosis within the parenchyma of the treated tissue.[17] Reports of treatment success range from 56 to 84%, and multiple treatments are often necessary. Adverse effects are seen in 10% of human patients and include pain and swelling at the ablation site and voice change.[8-12] Ethanol ablation has recently been reported in dogs as a treatment for PHP, with remission being achieved in 7 of 8 dogs.[13] Follow-up time for those dogs was 2 to 13 months. One treatment was required in 6 of the 7 successfully treated dogs, and 2 treatments were needed to achieve remission in the remaining dog.[13] Laryngeal paralysis that developed after chemical ablation was suspected in several dogs. Laryngeal paralysis was likely caused by dissection of ethanol along the fascial planes, causing inflammation of the recurrent laryngeal nerve.

Radiofrequency heat destroys tissue by causing thermal necrosis at the needle tip.[18] This offers multiple advantages, compared with ethanol ablation. First, radiofrequency damages a discrete quantity of tissue surrounding the noninsulated portion of the needle. Radiofrequency offers the additional advantage of not causing damage to regional vasculature. Blood flow through local vessels conveys heat away, sparing the vessel walls. In humans, radiofrequency heat ablation has a higher success rate than ethanol for ablation of masses, and fewer treatments are required to achieve remission.[14] Radiofrequency heat ablation has been employed in the treatment of multifocal hepatic masses, breast and nasal masses, and prostatic hypertrophy.[14,15,19-21] The disadvantage of radiofrequency heat ablation is equipment cost.

Findings from our study were similar to those reported for ethanol ablation,[13] with the exception of the 2 dogs in which we were unable to achieve adequate needle placement. In both of these dogs, the masses were small (< 0.5 cm in all dimensions). Retrospectively, we speculate that the masses continued to move away from the needle tip because the needle was too large; using a smaller needle may prevent this problem. However, pretreatment ultrasonography of the cervical area is recommended to identify dogs with small masses that may be poor candidates for this procedure.

One possible complication of this procedure is damage to structures in the vicinity of the parathyroid gland. Trauma to the recurrent laryngeal nerve may result in clinical signs as minor as a subtle voice change or as severe as laryngeal paralysis with respiratory compromise. Only 1 dog in our study had a transient voice change. Because of concerns regarding laryngeal paralysis, we chose not to ablate contralateral parathyroid masses during the same anesthetic procedure. Staging the procedures should allow recognition of abnormal recurrent laryngeal and arytenoid function on the side treated initially, minimizing the chance of bilateral laryngeal paralysis. Although not encountered here, puncture of the carotid artery by the needle and subsequent hemorrhage is an additional possible adverse effect of the heat ablation procedure.

Hypocalcemia is a concern whenever PHP is acutely resolved. Five of 8 successfully treated dogs in this study required treatment for hypocalcemia, compared with 1 of 7 dogs in the ethanol ablation study.[13] There is no clear explanation for this disparity. Dogs are expected to recover adequate parathyroid function after the atrophied parathyroid tissue has an opportunity to recover.[3] As with surgical removal of the abnormal parathyroid tissue, oral supplementation with vitamin D and calcium prior to treatment may be advisable in severely hypercalcemic dogs. Careful monitoring of serum ionized calcium concentration as performed in this study is recommended.

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[a]Animal Health Diagnostics Laboratory, Michigan State University, East Lansing, Mich.
[b]ATL Ultrasound Inc, Bothell, Wash.
[c]Beckton-Dickinson Infusion Therapy Services Inc, Sandy, Utah.
[d]Radiotherapeutics Inc, Redwood City, Calif.
[e]Roche Laboratories, Indianapolis, Ind.
[f]Bayer Corp, Norwood, Mass.
[g]DHT Dihydrotachysterol, Roxane Laboratories, Columbus, Ohio.
[h]Titrala, 3M Health Care Inc, St Paul, Minn.

References

1. DeVries SE, Feldman EC, Nelson RW, et al. Primary parathyroid gland hyperplasia in dogs: 6 cases (1982–1991). *J Am Vet Med Assoc* 1993;202:1132–1136.
2. Kruger JM, Osborne CA, Nachreiner RF, et al. Hypercalcemia and renal failure. *Vet Clin North Am Small Anim Pract* 1996;26:1417–1445.
3. Berger B, Feldman EC. Primary hyperparathyroidism in dogs: 21 cases (1976–1986). *J Am Vet Med Assoc* 1987;191:350–356.
4. Nyland T, Wisner E. Ultrasonography of the neck. In: Nyland T, Mattoon JS, eds. *Veterinary diagnostic ultrasound*. Philadelphia: WB Saunders Co, 1995;165–177.
5. Wisner ER, Mattoon JS, Nyland TG, et al. Normal ultrasonographic anatomy of the neck. *Vet Radiol Ultrasound* 1991;32:185–190.
6. Wisner ER, Nyland TG, Feldman EC, et al. Ultrasonographic evaluation of parathyroid glands in hypercalcemic dogs. *Vet Radiol Ultrasound* 1993;34:108–111.
7. Wisner ER, Pennick D, Biller DS, et al. High resolution parathyroid sonography. *Vet Radiol Ultrasound* 1997;38:462–466.
8. Karstrup S, Hegedus L, Holm H, et al. Ultrasonically guided chemical parathyroidectomy in patients with primary hyperparathyroidism: a follow-up study. *Clin Endocrinol (Oxf)* 1993;38:523–530.
9. Verges B, Cercueil J, Jacob D, et al. Results of ultrasonically guided percutaneous ethanol injection into parathyroid adenomas in primary hyperparathyroidism. *Acta Endocrinol (Copenh)* 1993;129:381–387.
10. Karstrup S, Hegedus L, Holm H, et al. Acute change in parathyroid function in primary hyperparathyroidism following ultrasonically guided ethanol injection into solitary parathyroid adenomas. *Acta Endocrinol (Copenh)* 1993;129:377–380.
11. Bennedbaek FN, Karstrup S, Hegedus L. Percutaneous ethanol injection therapy in the treatment of thyroid and parathyroid diseases. *Eur J Endocrinol* 1997;136:240–250.
12. Solbiati L. New applications of ultrasonography: interventional ultrasound. *Eur J Radiol* 1998;27:S200–S206.
13. Long CD, Goldstein RE, Hornof WJ, et al. Percutaneous ultrasound-guided chemical parathyroid ablation for the treatment of primary hyperparathyroidism in dogs. *J Am Vet Med Assoc* 1999;215:217–221.
14. Livraghi T, Goldberg NN, Lazzaroni S, et al. Small hepatocellular carcinoma: treatment with radio-frequency ablation versus ethanol ablation. *Radiology* 1999;210:655–661.
15. Jiao LR, Hansen PD, Havlik R, et al. Clinical short-term results of radiofrequency ablation in primary and secondary liver tumors. *Am J Surg* 1999;177:303–306.

16. Torrance AG, Nachreiner R. Human-parathormone assay for use in dogs: validation, sample handling studies, and parathyroid function testing. *Am J Vet Res* 1989;50:1123–1127.

17. Chow LT, Metreweli C, King WW, et al. Histological changes of parathyroid adenoma after percutaneous injection of ethanol. *Histopathology* 1997;30:87–89.

18. Cosman ER, Nashold BS, Ovelman-Levitt J. Theoretical aspects of radiofrequency lesions in the dorsal root entry zone. *Neurosurgery* 1984;15:945–950.

19. Utley DS, Goode RL, Hakim I. Radiofrequency energy tissue ablation for the treatment of nasal obstruction secondary to turbinate hypertrophy. *Laryngoscope* 1999;109:683–686.

20. Djavan B, Madersbacher S, Klingler HC, et al. Outcome analysis of minimally invasive treatments for benign prostatic hypertrophy. *Tech Urol* 1999;5:12–20.

21. Jeffrey SS, Birdwell RL, Ikeda DM, et al. Radiofrequency ablation of breast cancer: first report of an emerging technology. *Arch Surg* 1999;134:1064–1068.