Comparison of results of hormonal analysis of samples obtained from selected venous sites versus cervical ultrasonography for localizing parathyroid masses in dogs

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Objective—To compare a technique in which samples obtained from selected venous sites are analyzed for parathyroid hormone (PTH) concentration versus usefulness of cervical ultrasonography for localizing primary hyperparathyroidism (PHP) in dogs.

Design—Prospective study.

Animals—12 dogs with PHP.

Procedure—For each dog, blood samples were collected from the left and right jugular veins and 1 cephalic vein for determination of serum PTH concentration. Ultrasonography of the neck was performed in each dog. Each dog underwent exploratory surgery of the neck. Abnormal appearing parathyroid tissue was removed. Dogs were included in the study if serum calcium concentration decreased within 12 hours after surgery, hypercalcemia completely resolved within 96 hours after surgery, and serum calcium concentration was maintained within the reference range for at least 6 months after surgery.

Results—Serum PTH concentrations from the 3 veins were similar in 11 of 12 dogs with PHP. In 1 dog, the serum PTH concentration from the jugular vein ipsilateral to a parathyroid adenoma was greater than that from the contralateral jugular or cephalic vein. Ultrasonography correctly identified a parathyroid mass and its location in 10 of 11 dogs with a solitary abnormal parathyroid gland and in 1 dog in which both parathyroid glands were enlarged.

Clinical Implications—Surgeons may benefit from knowing the location of abnormal parathyroid tissue in dogs with PHP before surgical exploration. Ultrasonography has potential value for identifying and localizing abnormal parathyroid tissue, whereas sample collection from selected sites for PTH analysis is not likely to be helpful. (Am J Vet Med Assoc 1997;211:54-56)

Hypercalcemia is usually an abnormality serendipitously identified on serum biochemical analysis in dogs and is associated with various disease processes. Some of the disorders associated with hypercalcemia are lymphosarcoma, acute and chronic renal failure, vitamin D intoxicosis, apocrine gland carcinomas of the anal sac, multiple myelomas, hyperadrenocorticism, systemic mycoses, and primary hyperparathyroidism (PHP). Information from the history, physical examination, CBC, serum biochemical analysis, urinalysis, and abdominal ultrasonography were performed on each dog prior to inclusion. Dogs did not have abnormalities other than those attributable to untreated PHP (eg, polydipsia, polyuria, muscle weakness, poor appetite) and had a serum calcium concentration of ≥12 mg/dl on at least 3 separate days during a period of ≥30 days. After hypercalcemia was initially documented, serum calcium concentrations were greater than the reference range on all subsequent analyses prior to surgery. A thorough history, physical examination, CBC, serum biochemical analysis, urinalysis, thoracic radiography, and abdominal ultrasonography were performed on each dog prior to inclusion. Dogs did not receive any medication in the 3-month period preceding the initial evaluation.

Exploratory surgery of the thyroid area was completed in each dog. All visibly abnormal parathyroid tissue was removed and was histologically consistent with the diagnosis of PHP. All histologic examinations were performed by 1 investigator (PCK). Serum calcium concentration decreased in each dog within 12 hours after surgery, was within the reference range within 96 hours after surgery, and was maintained within the reference range for ≥6 months after surgery.

Study design—During the 48-hour period before surgery, blood samples were obtained from both jugular veins and from
1 cephalic vein of each dog. The 3 blood samples from each dog were obtained within a 10-minute period, were quickly centrifuged, and serum was harvested and stored at −20°C (−4°F) until assayed for PTH concentration. Samples from each dog were analyzed in the same assay. Cervical ultrasonography was performed on each dog within 48 hours preceding surgery. The thyroid/parathyroid area in each dog was evaluated for a mass or masses consistent with an enlarged parathyroid gland.7,10 Cervical ultrasonography was initially performed by the investigator (ERW) in 5 dogs and by a less experienced radiologist in 7 dogs. Six of these 7 dogs were reevaluated the same day or on the subsequent day by the investigator (ERW).

Surgeons performing exploratory surgery of the neck were not informed of ultrasonographic or serum PTH test results. Complete surgical exploration of both thyroid areas was performed in each dog. Abnormal appearing parathyroid tissue was removed. After surgery, serum calcium concentration was monitored every 12 hours for 3 days and then every 24 hours for 2 days. All dogs were discharged 7 to 8 days after surgery and were reexamined 7 and 21 days after discharge. Each dog was reexamined monthly for 6 months and then reexamined every 2 to 3 months.

Analytic methods—Serum PTH concentrations were determined, using a two-site immunoradiometric method that recognizes the amino- and carboxy-terminal ends of the intact molecule.9,10 Ultrasonography was performed, using a mechanical sector scanning transducer or a linear array transducer operating at a frequency of 10 MHz. Lesion measurements were obtained from ultrasonographic freeze-frame images by use of electronic calipers.

Results

The 12 dogs were 7 to 14 years old (mean, 11.3 years) and included 2 Keeshonds, 2 Shih Tzus, 1 Poodle, 1 German Shepherd Dog, 1 German Shorthaired Pointer, 1 Labrador Retriever, 1 Australian Shepherd Dog, and 3 mixed-breed dogs. Serum calcium concentrations for the 12 dogs prior to surgery were 12.1 to 19.1 mg/dL (mean, 15.8 mg/dL; median, 16.7 mg/dL). Serum ionized calcium concentrations for the 12 dogs prior to surgery were 1.49 to 1.93 mmol/L (mean, 1.73 mmol/L; median, 1.70 mmol/L). Serum PTH concentrations of samples obtained from the jugular veins and a cephalic vein of 11 dogs were similar (Table 1). Serum PTH concentration of a sample obtained from the right jugular vein from 1 dog was more than twice that of samples obtained from the left jugular and cephalic veins. It was determined during surgery that this dog had a parathyroid adenoma involving the right external parathyroid gland.

In 4 of 5 dogs that had only 1 cervical ultrasonographic examination, a parathyroid mass was visible. Masses were detected during both ultrasonographic examinations in 4 of the 7 other dogs. In the remaining 3 dogs, initial ultrasonographic examination did not reveal a mass, but a parathyroid mass was identified (by ERW) during the second examination.

Ultrasonographic observations in 11 of 12 dogs closely corresponded to observations made during surgery. Ten of these 11 dogs had a solitary hypocholic mass at the cranial pole of 1 thyroid gland, caudal pole of 1 thyroid gland, or within 1 thyroid gland; the remaining dog had masses associated with both thyroid glands. Ultrasonographically, parathyroid masses were 4 to 10 mm in diameter (Table 1). Parathyroid masses believed to be on the cranial pole of the thyroid gland on ultrasonography were located outside the thyroid gland, whereas parathyroid masses believed to be within or at the caudal pole of the thyroid gland were located within the affected thyroid gland.

Surgeons removed the thyroid gland when the parathyroid mass was located within the thyroid gland, whereas the thyroid gland was left intact when the parathyroid mass was located outside the thyroid gland. The dog that did not have a parathyroid mass visible on ultrasonography had an 8-mm parathyroid adenoma located outside the thyroid gland that was easily identified and removed during surgery. Parathyroid masses evaluated after removal were within 2 mm of the size determined during ultrasonography.

During surgery, 11 of 12 dogs had a solitary, large, discolored parathyroid mass. Seven masses were histologically diagnosed as parathyroid adenoma, 2 as low-grade parathyroid adenocarcinoma, and 2 as adenomatous hyperplasia of the parathyroid gland. One of the 12 dogs had 2 large, discolored parathyroid masses, which were histologically diagnosed as adenomatous hyperplasia (Table 1). A diagnosis of adenocarcinoma was made when there was evidence of capsular or vascular invasion. Criteria for distinguishing between adenomatous hyperplasia and adenoma have been described.11

Seven dogs with serum calcium concentrations ≥15.5 mg/dL prior to surgery were treated with vitamin D immediately after surgery. Vitamin D administration was slowly discontinued during a 2- to 4-month period. Five dogs with serum calcium concentrations between 12.0 and 15.4 mg/dL prior to surgery were not treated with calcium or vitamin D after surgery.

Discussion

Knowing the location of a tumor prior to surgery would be helpful. Although localization of parathyroid gland tumors in dogs can be determined by use of radio-

Table 1—Comparison of parathyroid hormone (PTH) concentration in samples obtained from the left and right jugular veins and a cephalic vein with results of ultrasonography for detection of parathyroid masses in 12 dogs

<table>
<thead>
<tr>
<th>Side of mass</th>
<th>No. of dogs</th>
<th>Total serum calcium concentration* (mg/dL)</th>
<th>Ionized serum calcium concentration† (mmol/L)</th>
<th>PTH concentration‡ (pmol/L)</th>
<th>Size of mass via ultrasonography (mm)</th>
<th>Histologic diagnosis of mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right</td>
<td>75</td>
<td>13.0–19.1</td>
<td>1.61–1.93</td>
<td>7.8–25.9</td>
<td>5.3–22.7</td>
<td>5.7–19.1</td>
</tr>
<tr>
<td>Left</td>
<td>4</td>
<td>12.1–18.5</td>
<td>1.48–1.85</td>
<td>5.0–20.2</td>
<td>3.1–32.1</td>
<td>3.4–21.2</td>
</tr>
<tr>
<td>Both</td>
<td>1</td>
<td>13.2</td>
<td>1.62</td>
<td>10.6</td>
<td>11.4</td>
<td>10.7</td>
</tr>
</tbody>
</table>

*Reference range, 9.2 to 11.4 mg/dL. †Reference range, 1.1 to 1.4 mmol/L. ‡Reference range, 1.0 to 9.0 pmol/L. | includes 1 dog in which the mass was not identified on ultrasonography.
nuclide imaging. The procedure is not widely available. Obtaining several venous blood samples is straightforward, and ultrasonography is becoming more available to veterinary practitioners. The purpose of obtaining 3 venous samples was based on venous drainage of the parathyroid glands into the jugular veins. It was assumed that a dog with autonomously secreting parathyroid tissue (adenoma, adenocarcinoma, or adenomatous hyperplasia) would have similar serum concentrations of PTH in the contralateral jugular vein and a cephalic vein, but that the PTH concentration in blood from the jugular vein ipsilateral to autonomously secreting tissue would be obviously greater.

As results from each dog with PHP became available, this hypothesis did not appear to be correct. Because we believed that we might be obtaining blood at a point too proximal in the jugular vein, we attempted to obtain blood from as close to the thoracic inlet as possible. A gradient between the jugular vein ipsilateral to the autonomously secreting tissue and the contralateral vein remained undetectable. In 2 dogs, samples were collected by the surgeons after the thyroid glands were exposed in a specific attempt to obtain blood that certainly had drained from the parathyroid gland. However, serum PTH concentrations from these 2 dogs were not different from concentrations in samples obtained contemporaneously prior to surgery. Thus, use of selective venous blood sample collection for obtaining serum for PTH assay prior to surgery in an attempt to determine the location of autonomously secreting parathyroid tissue was successful in only 1 of 12 dogs. Alternative methods for collection of blood samples may provide more definitive results.

Ultrasonography, similar to many diagnostic tools used in veterinary medicine, is operator dependent. The skill of the individual performing the examination is a major factor in the value of the results. Five radiologists conducted cervical ultrasonography on the 12 dogs of this report. In 8 dogs, a mass in the area of the thyroid gland was identified on initial evaluation. In 3 dogs, however, a parathyroid mass was not observed on initial evaluation. These dogs were reexamined later that day or on the next day by a radiologist (ERW) with more experience who was able to detect a parathyroid mass. In 1 dog, a mass was not detected during cervical ultrasonography, which was performed by a relatively inexperienced radiologist. However, that dog was not reexamined. In any case, a single ultrasonographic examination may not consistently reveal a parathyroid mass in dogs with PHP. Further, radiologists experienced in cervical ultrasonography may likely have greater success in detecting small masses than radiologists with less experience. The diagnosis of PHP was established in each dog prior to obtaining multiple venous blood samples and prior to cervical ultrasonography. Ultrasonography is not recommended as a tool for diagnosing PHP, but as a localization procedure after confirmation of the disease. Although clinically healthy dogs do not have sonographically detectable hypoechoic masses in the thyroid area, studies to date do not justify use of ultrasonography as a diagnostic test. A single ultrasonographic examination performed on a dog with PHP should be viewed as a potentially helpful localization procedure and should not replace appropriate diagnostic protocols. Regardless of ultrasonographic results, however, complete exploration of the thyroid/parathyroid area is warranted in any dog undergoing surgery to resolve PHP. Each of the 12 dogs in this study had abnormal parathyroid tissue observed and removed during surgery. In 4 of these dogs, however, the surgeon with primary responsibility for the dog requested the opinion of a more experienced surgeon and an internist before removing any tissue. Thus, although all 12 dogs were managed appropriately during surgery, previous experience was beneficial. Because this disease is now well recognized, surgeons with less experience will likely benefit from information gained during ultrasonography, whereas surgeons with more experience may not benefit from this information.

References


