Idiopathic Hypercalcemia in Cats

A.M. Midkiff, D.J. Chew, J.F. Randolph, S.A. Center, and S.P. DiBartola

Unexplained hypercalcemia has been increasingly recognized in cats since 1990. In some instances, hypercalcemia has been associated with calcium oxalate urolithiasis, and some affected cats have been fed acidifying diets. We studied the laboratory findings, clinical course, and treatment of 20 cats with idiopathic hypercalcemia. Eight (40%) of the cats were longhaired and all 14 cats for which adequate dietary history was available had been fed acidifying diets. Clinical signs included vomiting (6 cats), weight loss (4 cats), dysuria (4 cats), anorexia (3 cats), and inappropriate urinations (3 cats). Hypercalcemia was mild to moderate in severity, and serum parathyroid hormone concentrations were normal or low. Serum concentrations of phosphorus, parathyroid hormone–related peptide, 25-hydroxycholecalciferol, and calcitriol were within the reference range in most cats. Diseases commonly associated with hypercalcemia (eg, neoplasia, primary hyperparathyroidism) were not identified despite thorough medical evaluations and long-term clinical follow-up. Azotemia either did not develop (10 cats) or developed after the onset of hypercalcemia (3 cats), suggesting that renal failure was not the cause of hypercalcemia in affected cats. Seven of 20 cats (35%) had urolithiasis, and in 2 cats uroliths were composed of calcium oxalate. Subtotal parathyroidectomy in 2 cats and dietary modification in 11 cats did not result in resolution of hypercalcemia. Treatment with prednisone resulted in complete resolution of hypercalcemia in 4 cats.

Key words: Acidifying diet; Calcium; Calcium oxalate; Parathyroid hormone; Urolithiasis.

Materials and Methods

Medical records of cats with unexplained hypercalcemia presented to The Ohio State University Veterinary Teaching Hospital (8), Cornell University College of Veterinary Medicine (6), and selected private practices (6) were reviewed. Criteria evaluated for all cats in the study included serum total and ionized calcium, parathyroid hormone (PTH), creatinine, urea nitrogen, phosphorus, and albumin concentrations. Enzyme immunoassay criteria included either a serum total calcium concentration or serum ionized calcium concentration above the upper limit of the normal reference range (11.5 mg/dL and 5.5 mg/dL, respectively). For many cats, results of urinalysis, serum thyroxine concentration, bone marrow cytology, blood gas analysis, abdominal and thoracic radiography, abdominal ultrasonography, parathyroid hormone–related polypeptide (PTHrP), serum 25-hydroxycholecalciferol (calcidiol) and 1,25-dihydroxycholecalciferol (calcitriol) assays, and feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV) enzyme-linked immunosorbent assay (ELISA) tests also were available. Serum chemistries were performed by routine automated techniques. Serum thyroxine concentrations were determined by chemiluminescence. Serum PTH, PTHrP, 25-hydroxycholecalciferol, and serum ionized calcium concentrations were determined at the Michigan State University Endocrine Diagnostic Laboratory. Serum PTH concentration was measured by an immunoradiometric assay for intact PTH that previously has been validated for use in cats. Serum PTHrP concentration was measured by an immunoradiometric assay for PTHrP 1-84 that previously has been used in cats with adenocarcinomas. Serum 25-hydroxycholecalciferol concentration was measured by a commercially available radioimmunoassay. Serum calcitriol concentrations were measured by Dr Bruce Hollis of the Division of Pediatrics at the Medical University of South Carolina by a previously described radioimmunoassay. Serum samples from 3 cats were analyzed for calcitriol by the Nichols Institute. Two cats underwent surgical exploration of the neck and subtotal parathyroidectomy, 6 cats were treated with orally administered glucocorticoids, and 11 cats underwent dietary modification.

Results

Signalment and Diet

Cats ranged from 2.0 to 13.4 years in age, with a mean age of 5.8 years and median age of 5.4 years at the onset of hypercalcemia. Twelve cats were males and 8 were females; all were neutered. Eleven cats were Domestic Short-hairs, 4 were Domestic Longhairs, 2 were Himalayans, 1 was a Burmese, 1 was a Maine Coon, and another was a Persian. Two cats were related and living in the same household, whereas 2 other cats were not related but shared the same environment. Of the 14 cats for which diet history was available, all were fed acidifying diets designed to minimize struvite crystalluria and urolithiasis. The cats were fed ProPlan Light (1), Meow Mix and Chef’s Blend (1),
One cat was treated for several years after diagnosis of hypercalcemia and went on to develop pancreatitis 20 months after diagnosis of hypercalcemia. Another cat had undergone ligation of a portosystemic shunt approximately 2 years before it developed hypercalcemia and was receiving L-thyroxine supplementation. Two sibling cats developed peripheral vestibular disease 5 months before the onset of hypercalcemia. One cat had undergone cystotomy to remove struvite calculi 50 months before the onset of hypercalcemia. Both kidneys were small and more than normal size based on abnormal pal¬¬pation, including the left kidney of 1 cat that previously had undergone right nephrectomy. Both kidneys were smaller than normal in 5 cats. Systolic heart murmurs of grades II–IV were auscultated in 5 cats at presentation, and a grade III/VI systolic murmur developed in another cat approximately 4 years after the onset of hypercalcemia.

Additional physical examination findings included urethral obstruction in 1 cat, and palpable thyroid nodules in 2 cats. Two sibling cats developed peripheral vestibular disease 10–28 months after the onset of hypercalcemia. One cat developed hypothyroidism 1 year before the onset of hypercalcemia and was receiving L-thyroxine supplementation. The affected cat was presented for evaluation of lethargy, dry hair coat, and seborrhea sicca. This cat also had a cystotomy to remove struvite calculi 50 months before the onset of hypercalcemia. One cat was treated for sclerosing cholangitis for 19 months before hypercalcemia developed. Another cat had undergone ligation of a portosystemic shunt approximately 2 years before it developed hypercalcemia and went on to develop pancreatitis 20 months after diagnosis of hypercalcemia.

### Laboratory Evaluation

Serum total calcium concentrations ranged from 10.6 to 14.1 mg/dL (mean = 12.4 mg/dL, SD = 0.9 mg/dL; reference range, 8.6–11.5 mg/dL), whereas serum ionized calcium concentrations ranged from 5.9 to 7.6 mg/dL (mean = 6.6 mg/dL, SD = 0.4 mg/dL; reference range, 4.0–5.5 mg/dL). Serum PTH concentrations were measured in 17 cats and ranged from <0.1 to 2.5 pmol/L (mean = 1.1 pmol/L, SD = 0.8 pmol/L; reference range, <0.1–4 pmol/L). Six cats had PTH concentrations <0.1 pmol/L.

PTHrP was measured in 11 cats and ranged from <0.2 to 3.7 pmol/L (mean = 0.5 pmol/L, SD = 1.2 pmol/L; reference range, <0.2 pmol/L). Nine cats had PTHrP concentrations <0.2 pmol/L. Serum 25-hydroxycholecalciferol concentrations were measured in 17 cats and ranged from 81 to 321 nmol/L (mean = 151 nmol/L, SD = 63 nmol/L). Serum 25-hydroxycholecalciferol concentrations in 21 healthy young adult cats ranged from 88 to 168 nmol/L (Graham, personal communication). Twelve of 17 hypercalcemic cats had serum 25-hydroxycholecalciferol concentrations within or below this reference range. Serum calcitriol concentrations were measured in 7 cats and ranged from <5 to 75 pg/mL (mean = 28 pg/mL, SD = 24 pg/mL). Mean serum calcitriol concentrations in normal adult cats have been reported to be 30 pg/mL in 20

### Measured Value

<table>
<thead>
<tr>
<th>Reference Range</th>
<th>Measured Value</th>
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<td>(mean ± SD, range)</td>
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- Survival after diagnosis (years)
- TCa (mg/dL)
- ICa (mg/dL)
- PTH (pmol/L)
- PTHrP (pmol/L)
- 25(OH)D3 (nmol/L)
- 1,25(OH)2D3 (pg/mL)
- Age hypercalcemia recognized (years)
- Total survival after diagnosis (years)
- Total serum total calcium concentration
- Total serum ionized calcium concentration
- Total serum parathyroid hormone
- Total serum parathyroid hormone-related peptide concentration
- Total serum 25-hydroxycholecalciferol concentration
- Total serum 1,25-hydroxycholecalciferol concentration

NA, not applicable; TCa, serum total calcium concentration; ICa, serum ionized calcium concentration; PTH, serum parathyroid hormone concentration; PTHrP, serum parathyroid hormone–related peptide concentration; 25(OH)D3, serum 25-hydroxycholecalciferol concentration; 1,25(OH)2D3, serum calcitriol concentration.

- Survival time after diagnosis is given as the minimum number of years because several cats were alive at the time of writing.
- Eleven cats.
- Seventeen cats.
- Seven cats.
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Phosphorus concentrations ranged from 2.7 to 5.4 mg/dL (mean = 4.4 mg/dL, SD = 0.7 mg/dL; reference range, 2.7–6.5 mg/dL), whereas serum albumin concentrations ranged from 2.8 to 4.3 g/dL (mean = 3.5 g/dL, SD = 0.4 g/dL; reference range, 2.7–4.1 g/dL).

Three cats had azotemia or chronic renal failure (CRF) that preceded development of hypercalcemia by 6–10 months and, in 1 of these cats, azotemia resolved 2 months before the onset of hypercalcemia and did not recur. Azotemia was discovered concurrently with hypercalcemia in 5 cats. Twelve cats had no azotemia or evidence of CRF before the onset of hypercalcemia, but 3 of these cats developed azotemia or CRF 18–40 months later.

Venous blood gas analysis was performed in 3 cats. One cat had CRF with a blood pH of 7.28, Po2 of 43.6 mm Hg, PaO2 of 49 mm Hg, blood bicarbonate (HCO3−) concentration of 20 mEq/L, total CO2 (TCO2) of 21 mEq/L, and a base excess (BE) of −6 mEq/L. The 2nd cat had a blood pH of 7.33, PaCO2 of 38.7 mm Hg, PaO2 of 46.4 mm Hg, HCO3− of 19.6 mEq/L, TCO2 of 20.8 mEq/L, and a BE of −5.4 mEq/L. The 3rd cat had a blood pH of 7.38, PaCO2 of 35.4 mm Hg, PaO2 of 42.6 mm Hg, HCO3− of 20.2 mEq/L, TCO2 of 21.3 mEq/L, and a BE of −3.8 mEq/L.

Serum thyroxine concentration was measured in 11 cats. Serum thyroxine concentration was within the reference range in 9 of these 11 cats, including 1 cat with hypothyroidism that was receiving treatment with L-thyroxine. In this cat, the diagnosis of hypothyroidism was made based on serum thyroxine concentrations of 0.44 μg/dL before and 0.60 μg/dL after thyrotropin administration. Two other cats had slightly low serum thyroxine concentrations (0.87 and 0.90 μg/dL), which were attributed to the effect of nontoxic nodules. Neither of the 2 cats with slightly low serum thyroxine concentrations had been treated by subtotal parathyroidec-tomy.

Urine samples were collected from 17 cats (8 by cystocentesis, 5 by unrecorded method, 3 by voiding, and 1 by catheterization). Urine specific gravity ranged from 1.012 to 1.060 (mean = 1.036, SD = 0.013). Urine protein dipstick determinations were negative in 4 cats, 10–30 mg/dL in 6 cats, 30–100 mg/dL in 5 cats, 100–500 mg/dL in 1 cat, and >500 mg/dL in 1 cat. Crystalluria was identified in 9 cats. Five of these cats had struvite crystalluria, 3 had calcium oxalate crystalluria, and 1 had amorphous crystalluria. Hematuria was detected in 9 cats, but pyuria was not detected in any cat. Of the 9 cats with hematuria, urine had been collected by cystocentesis in 5, voiding in 2, catheterization in 1, and in the remaining cat the method of collection was not recorded. Urine pH ranged from 5.5 to 7.0 (mean = 6.2, SD = 0.4).

The fractional excretion of calcium was calculated in 4 cats by spot urine samples, and values of 0.80, 1.82, 1.90, and 2.76% were obtained. Normal values for fractional excretion of calcium in 30-week-old cats were reported to be 0.06 ± 0.05% and values determined by 72-hour urine samples in 5 young adult cats were 0.05–0.14%.

Results of thoracic radiographs were normal in 9 of 13 cats and disclosed generalized cardiomegaly in 4 cats. On abdominal radiography, normal-sized kidneys were identified in 6 of 9 cats and small kidneys were observed in 3 of 9 cats. Seven cats had radiopaque calculi, and nephrocalcinosis was identified in 1 cat. Three cats had only renal calculi, and 1 cat had only cystic calculi. One cat had renal and ureteral calculi, another had ureteral and cystic calculi, and 1 cat had uroliths visible in the kidney, ureter, and bladder. Two cats had cystotomies performed to remove their cystic calculi, and in both cats the calculi were composed of 100% calcium oxalate. Abdominal ultrasonography in 15 cats disclosed urinary calculi in 5, with 3 cats having only renal calculi and 2 cats having both renal and cystic calculi. Ten of these 15 cats had normal-sized kidneys and 5 had small kidneys. Three cats had irregularly shaped kidneys, nephrocalcinosis was identified in 5 cats, and renal pelvic dilatation was evident in 2 cats. Results of ultrasonography of the cervical region were normal in 3 cats in which it was performed. Results of a pertechnetate thyroid scan were normal in another cat. Ultrasonography of the neck was not performed in the cats that underwent exploratory cervical surgery.

FIV and FeLV ELISA tests were performed in 10 and 14 cats, respectively, and all test results were negative. Cytologic evaluation of bone marrow aspirates was normal in the 3 cats in which bone marrow aspirates were performed.

Two cats underwent surgical exploration of the neck and removal of 2 or 3 of their 4 parathyroid glands and associated thyroid tissue. The parathyroid glands appeared normal grossly and were normal on histopathologic examination. In 1 cat, hypercalcemia resolved 2 days after surgery (serum total calcium concentration, 8.0 mg/dL; serum ionized calcium concentration, 4.8 mg/dL), but returned by the 3rd postoperative day (serum total calcium concentration, 11.0 mg/dL; serum ionized calcium concentration, 6.5 mg/dL). One week later, serum total calcium concentration was 12.4 mg/dL in this cat. In another cat, serum total calcium concentration also decreased to within normal limits 2 days after surgery (from 13.3 mg/dL to 10.8 mg/dL), but increased by the 5th postoperative day to 12.0 mg/dL. The serum total calcium concentration in this cat was 11.7 mg/dL 3 months postoperatively.

Diagnosis and Treatment

A diagnosis of idiopathic hypercalcemia in these cats was made on the basis of abnormally high serum total or ionized calcium concentration, the cause of which remained unknown after extensive medical evaluation. Treatment consisted of dietary modification, orally administered glucocorticoids, or both.

Eleven cats were treated by dietary modification. Three cats were fed k/d, 3 were fed w/d, 3 were fed c/do, and 1 cat was fed a combination of k/d and w/d, and 1 cat was fed IVD Venison and Potato. None of the 7 cats fed k/d or w/d and neither of the 2 fed c/do experienced a decrease in serum total or ionized calcium concentrations. The cat fed IVD Venison and Potato, which previously was fed Whiskas, experienced a reduction in serum total calcium concentration from 12.8 to 9.8 mg/dL, but no reduction in serum ionized calcium concentration was identified. The response of the other cat fed c/do to diet change alone could not be determined because of concurrent treatment with prednisone, but this cat also experienced a reduction in serum total calcium concentration from 12.3 to 10.4 mg/dL.
whereas serum ionized calcium concentration remained abnormally high.

Six cats (including the previously mentioned cat that also underwent dietary modification with c/do) were treated with prednisone. Of the 5 cats that did not undergo concurrent dietary modification, 1 cat experienced a decrease in both serum total and ionized calcium concentrations from 12.0 to 10.5 mg/dL and 6.8 to 5.3 mg/dL, respectively, while receiving 12.5 mg of prednisone daily. This cat maintained normocalcemia with a mean total serum calcium concentration of 10.3 mg/dL at this dose for 27 months, but the total serum calcium concentration increased to 11.0 mg/dL within 2 weeks of decreasing the prednisone dose to 6.25 mg per day. Therefore, the dose was returned to 12.5 mg per day. Another cat receiving 10 mg of prednisone daily also experienced a decrease in serum total and ionized calcium concentrations to within normal limits from 11.9 to 10.4 mg/dL and 6.3 to 5.5 mg/dL, respectively. However, this cat demonstrated no recurrence of hypercalcemia 3 weeks after discontinuing treatment with prednisone, after 19 months of successful therapy. The 3rd cat (also receiving 10 mg of prednisone daily) experienced a reduction in serum total calcium concentration from 13.2 to 11.4 mg/dL, but had no reduction in serum ionized calcium concentration with concentrations remaining at 7.0 and 6.7 mg/dL. In contrast, the 4th cat treated with prednisone (also 10 mg/d) experienced a reduction in serum ionized calcium concentration from 1.8 to 1.4 mmol/L (from 7.2 to 5.6 mg/dL), but serum total calcium concentration was not determined. The 5th cat treated with prednisone received 5 mg daily and experienced a decrease in serum total calcium concentration from 12.9 to 11.4 mg/dL. Posttreatment serum ionized calcium concentration was not determined for this cat.

Discussion

Hypercalcemic cats in the present study ranged from 2 to 13 years of age. The mean (5.8 years) and median (5.4 years) ages were similar to those reported recently for 5 cats with hypercalcemia and oxalate urolithiasis, but the cats of the present study were younger than those reported in a recent retrospective study of hypercalcemic cats in which the mean and median ages of affected cats were 8.8 and 9.0 years, respectively. Eight of 20 (40%) cats in the present study were longhaired, a finding identical to that reported in another report. Domestic Longhair cats represent 7% of cats examined at the Veterinary Teaching Hospital at Cornell University and 14% of the cats examined at the Ohio State University Veterinary Teaching Hospital. Males outnumbered females in the present report whereas 4 of 5 cats in another study were females. Nearly equal numbers of affected male and female cats with hypercalcemia were reported in another recent study. Anorexia and lethargy were the most common clinical findings in cats with hypercalcemia in a recent retrospective study. Polydipsia and polyuria were reported in 17 (24%) of the 71 hypercalcemic cats, signs of lower urinary tract disease were identified in 16 (23%), and vomiting was a client complaint in 13 (18%) of the affected cats. All of the cats in another study of hypercalcemia and calcium oxalate urolithiasis were presented for signs of lower urinary tract disease. The most common clinical signs in the cats of the present study were vomiting (6 of 20, 30%), weight loss (4 of 20, 20%), and dysuria (4 of 20, 20%). Anorexia (3 of 20, 15%) and lethargy (2 of 20, 10%) were reported less commonly in the cats of the present study.

The magnitude of hypercalcemia in the cats of the present study varied considerably, but it generally was moderate in severity. Based on serum total calcium concentrations, hypercalcemia was considered mild (11.5–12.0 mg/dL) in 8 of 20 (40%) cats, moderate (12.1–14.0 mg/dL) in 11 of 20 (55%) cats, and severe (>14.0 mg/dL) in 1 cat. Based on serum ionized calcium concentrations, hypercalcemia was considered mild (5.6–6.0 mg/dL) in 2 of 20 (10%) cats, moderate (6.1–7.0 mg/dL) in 16 of 20 (80%) cats, and severe (>7.0 mg/dL) in 2 of 20 (10%) cats. Serum phosphorus concentrations were within the reference range in all 20 cats. Mild reductions in serum phosphorus would have been expected with primary hyperparathyroidism and increased concentrations could have been anticipated in some cats with CRF.

Results of assays for serum concentrations of PTH, PTHrP, 25-hydroxycholecalciferol, and 1,25-dihydroxycholecalciferol helped eliminate many known causes of hypercalcemia as diagnostic possibilities in the cats of the present study. One cat had increased serum PTHrP concentration (3.7 pmol/L). The reason for the abnormally high concentration of PTHrP in this cat could not be determined, but the cat survived more than 3 years after the onset of hypercalcemia, making underlying malignancy an unlikely explanation for the high PTHrP concentration. Five cats had serum 25-hydroxycholecalciferol concentrations above the upper limit of the reference range (ie, >168 nmol/L). Unlike serum calcitriol concentration, the serum concentration of 25-hydroxycholecalciferol is not closely regulated, and variation in the concentrations of 25-hydroxycholecalciferol may have reflected differences in dietary intake of vitamin D. Vitamin D toxicosis was not a likely explanation for the increased serum 25-hydroxycholecalciferol concentrations in these cats. The observed increases were mild (less than twice the upper limit of the reference range), whereas 25-hydroxycholecalciferol concentrations in dogs with vitamin D toxicosis typically are 5–20 times the reference range value. One cat had a serum calcitriol concentration of 75 pg/mL (approximately twice the reference range value). Serum calcitriol concentration normally is closely regulated, and the explanation for the increased calcitriol concentration in this cat could not be determined. Hypercalcemia (possibly due to calcitriol synthesis by mononuclear cells) has been reported in 4 dogs and 1 cat with granulomatous disease. The cat of the present study with increased calcitriol concentration lived 2 years after the onset of hypercalcemia, and at postmortem examination neither neoplasia nor granulomatous disease was identified.

Urinary fractional excretion of calcium was abnormally high in 4 affected cats based on values published for healthy 30-week-old cats and young adult cats. However, whether this degree of urinary calcium excretion is excessive for hypercalcemic cats is unknown (ie, such excretion may represent an appropriate physiologic response to hypercalcemia). Urinary fractional excretion of calcium de-
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terminated by spot urine samples correlates poorly with results of 72-hour urinary excretion of calcium in cats. Concluding that cats with idiopathic hypercalcemia are hypercalciuric would be premature.

Primary hyperparathyroidism is an uncommon cause of hypercalcemia in cats. Serum PTH concentrations in cats with primary hyperparathyroidism were abnormally high or within the reference range, and most affected cats had palpable cervical masses. Calcium oxalate urolithiasis complicated primary hyperparathyroidism in at least 1 of these cats. In a recent retrospective study of hypercalcemia in cats, 4 had primary hyperparathyroidism and 3 of these cats had serum PTH concentrations within the reference range. In the present study, serum PTH concentrations were at the lower end of the reference range. Serum PTH concentrations were <1 pmol/L in 7 cats (0 pmol/L in 6 cats and 0.9 pmol/L in 1 cat), a finding not compatible with primary hyperparathyroidism. In the remaining 13 cats, serum PTH concentrations were between 1.0 and 2.5 pmol/L (reference range, 0–4 pmol/L), which could be considered inappropriate in animals with ionized hypercalcemia. However, complete inhibition of PTH secretion is not achieved even in the presence of severe hypercalcemia. Furthermore, cervical ultrasonography in 3 cats and surgical exploration of the neck in 2 additional cats did not disclose parathyroid tumors. In the 2 cats that underwent subtotal parathyroidectomy, transient resolution of hypercalcemia occurred but hypercalcemia recurred within a few days of surgery. Thus, primary hyperparathyroidism is unlikely to be the cause of hypercalcemia in the cats of the present report.

The most common pathologic cause of hypercalcemia in cats is neoplasia including lymphosarcoma, squamous cell carcinoma, and multiple myeloma. Neoplasms were not evident on physical examination of the cats in the present study. Furthermore, abdominal ultrasonography (15 cats), thoracic radiography (13 cats), abdominal radiography (9 cats), and bone marrow cytology (3 cats) failed to disclose evidence of neoplasia. Five of the cats in the present study have died or been euthanized, and no evidence of neoplasia was found in the 2 cats on which a postmortem examination was performed. Fifteen of the 20 cats described here were alive up to 7 years or more after diagnosis of hypercalcemia (2 cats >7 years, 1 cat >5 years, 3 cats >4 years, 1 cat >3 years, 4 cats >2 years, and 4 cats >1 year). Of the cats that died or were euthanized, 1 survived for 4 years after diagnosis, 1 survived for 3 years, 2 survived for 2 years, and 1 survived for 1 year. Without treatment, cats with lymphosarcoma (the malignancy most commonly associated with hypercalcemia) usually survive less than 30 days. Prolonged survival in the cats of the present study suggests that neoplasia is an unlikely cause of hypercalcemia in these cats. Also, serum concentrations of PTHrP were undetectable in 9 of 11 (82%) cats evaluated.

Hypercalcemia may occur in dogs with hypoadrenocorticism and has been reported in at least 1 cat with this disease. None of the cats in the present study had clinical or laboratory findings suggestive of hypoadrenocorticism, and results of an adrenocorticotropic hormone stimulation test in 1 cat were normal. Hypercalcemia also has been reported in cats that have ingested cholecalciferol-containing rodenticides. No history of rodenticide ingestion was noted in any of the cats in the present study, serum 25-hydroxycholecalciferol concentrations were within the reference range in 12 of 17 cats (71%), and serum phosphorus concentrations were within the reference range in all cats, making hypervitaminosis D an unlikely cause of hypercalcemia in the cats of this report.

Most dogs and cats with CRF have serum total calcium concentrations within the reference ranges, but hypercalcemia occasionally is observed. Mild hypercalcemia has been reported in 11.5% of cats with CRF with the highest serum total calcium concentration being 12.7 mg/dL. In a recent retrospective study of hypercalcemic cats, the most common disease associations were neoplasia, renal failure, and urolithiasis. In that study, the mean serum total calcium concentration in 18 hypercalcemic cats with renal failure was 11.5 mg/dL. In 13 of 20 hypercalcemic cats in the present study, azotemia either did not develop during their clinical course (10 cats) or developed after the onset of hypercalcemia (3 cats). These observations suggest that renal disease and failure were not the cause of hypercalcemia in most affected cats. However, in at least 3 cats, hypercalcemia potentially could have contributed to the development of azotemia and CRF. The occurrence of serum PTH concentrations within the reference range in the cats of the present report also is not consistent with renal secondary hyperparathyroidism that would be expected in cats with CRF. In 1 study, mean plasma PTH concentration was 39.6 pg/mL in 15 asymptomatic cats with compensated CRF; 118.6 pg/mL in 39 symptomatic cats with decompensated CRF; and 348.6 pg/mL in 26 dehydrated, anorexic cats with endstage CRF (reference range, 2.9–25.5 pg/mL). In another study of 13 cats treated for CRF, mean plasma PTH concentration before dietary phosphorus restriction was 137.8 pg/mL, and the lowest PTH concentration observed was 40.0 pg/mL.

In recent studies, hypercalcemia has been reported in cats with oxalate urolithiasis. Results reported from the University of Minnesota Urolith Center indicate that mild hypercalcemia (11.5–13.5 mg/dL) has been observed in 35% of cats with calcium oxalate uroliths. In a series of case reports, 5 cats with hypercalcemia and calcium oxalate urolithiasis presented for evaluation of lower urinary tract signs (eg, pollakiuria, hematuria), and either had been fed acidifying diets (c/d, s/d) or received urinary acidi
cators (D,L-methionine). Serum total and ionized calcium concentrations were moderately high and serum PTH concentrations were 0–1.3 pmol/L. Hypercalcemia resolved after discontinuation of acidification therapy or acidifying diet in these 5 cats. In a recent retrospective study of 71 hypercalcemic cats, signs of lower urinary tract disease (eg, pollakiuria, hematuria, stranguria) were reported in 16 of 71 (22%) cats, urolithiasis was found in 11 of 16 (69%) cats, and calculi were composed of calcium oxalate in 8 of 11 (73%) cats. Four of 9 (44%) cats for which dietary history was available had been fed acidifying diets. Nine of the 11
Familial benign hypercalcemia (FBH) is an autosomal dominant trait in humans characterized by lifelong nonprogressive hypercalcemia. Serum PTH concentrations are within the reference range or mildly increased despite the presence of hypercalcemia, and renal tubular reabsorption of calcium is increased. Additional laboratory features include normal or slightly decreased serum phosphorus and calcitriol concentrations, normal serum 25-hydroxycholecalciferol concentrations, and urinary fractional excretion of calcium ≤1%. Unlike patients with primary hyperparathyroidism, those with FBH have normal bone mineral density and rarely develop urolithiasis. They generally have few if any clinical manifestations, and their hypercalcemia does not respond to administration of glucocorticoids. In most cases, FBH is caused by an inactivating mutation in one copy of the gene for the calcium-sensing receptor.

Cats with idiopathic hypercalcemia described in this report resemble humans with FBH in some ways but not others. Similarities include hypercalcemia with normal serum PTH concentration; normal gross and histologic morphology of parathyroid glands; normal or slightly low serum concentrations of phosphorus, calcitriol, and 25-hydroxycholecalciferol; and failure to achieve normocalcemia after subtotal parathyroidectomy. Potentially important dissimilarities between humans with FBH and cats with idiopathic hypercalcemia include presence of calcium oxalate urolithiasis, fractional excretion of calcium >1%, and therapeutic response to glucocorticoids in affected cats.

Futher evaluation of idiopathic hypercalcemia in cats will require balance studies that include determination of dietary intake, intestinal absorption, fecal excretion, bone resorption, and urinary excretion of calcium. Alkali therapy should also be considered to assess the role of dietary acidification and chronic subclinical metabolic acidosis in this syndrome, and treatment with biphosphonates may elucidate the role of bone resorption.

Footnotes

1 Cite Test, Idexx Corporation, Westbrook, ME
2 Diagnostic Products Corporation, Los Angeles, CA
3 INCSTAR Corporation, Stillwater, MN
4 Nichols Institute, San Juan Capistrano, CA
5 ProPlan Light, Meow Mix, and CNM, Ralston Purina Co, St Louis, MO
6 Chef’s Blend, Fancy Feast, and Friskies, Friskies, St Joseph, MO
7 Iams and Iams Less Active, Iams Co, Dayton, OH
8 Whiskas, Waltham USA Inc, Vernon, CA
9 Max Cat and Nutrocat, Nutro Products Inc, City of Industry, CA
10 IVD Feline Duck and Potato and IVD Venison and Potato, Nature’s Recipe, Corona, CA
11 Science Diet, w/d, k/d, c/do, and s/d, Hill’s Pet Nutrition Inc, Topeka, KS
12 Dad’s, Dad’s Product’s Co Inc, Meadville, PA
13 Fractional excretion of calcium (%) = ([urine calcium]/[serum creatinine])/[serum calcium][urine creatinine]) × 100

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References


Abstracts from Current Literature: Journal of Clinical Microbiology

Experimental Inoculation with Human Granulocytic Ehrlichia Agent Derived from High- and Low-Passage Cell Culture in Horses.


*Journal of Clinical Microbiology* 2000;38:1276–1278 (abstract only).

We report the successful infection throughout intravenous inoculation with low and high passage of in vitro-grown human granulocytic ehrlichiosis (HGE) agent in horses. Differences in disease severity but not in incubation time, hematological changes, PCR detection, ehrlichial load, seroconversion time, and titer range were noted between horses infected with a low and a high passage of in vitro-grown HGE agent.

Helmintic Transmission and Isolation of *Ehrlichia risticii*, the Causative Agent of Potomac Horse Fever, by Using Trematode Stages from Freshwater Stream Snails.


*Journal of Clinical Microbiology* 2000;38:1293–1297 (abstract only).

We report successful helminthic transmission of *Ehrlichia risticii*, the causative agent of Potomac horse fever, using trematode stages collected from *Juga yrekaensis* snails. The ehrlichial agent was isolated from the blood of experimentally infected horses by culture in murine monocytic cells and identified as *E. risticii* ultrastructurally and by characterization of three different genes.