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Survival and Prognostic Indicators for Cycad Intoxication in Dogs

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Background: Cycad palms are commonly used in landscaping and ingestion by dogs can cause disease or death.

Objectives: Determine the morbidity and case fatality of cycad palm toxicosis in dogs from Louisiana, and examine putative prognostic factors.

Animals: Thirty-four client-owned dogs with confirmed cycad palm toxicosis between 2003 and 2010.

Methods: Retrospective cohort study. Search of all medical records for animals with cycad palm toxicosis.

Results: Seventeen of 34 (50%) dogs died or were euthanized as a direct consequence of cycad intoxication. There were no differences in presenting signs and physical examination findings between survivors and nonsurvivors. Nonsurvivors had higher serum alanine transaminase activity (median 196 U/L; range 16–4,123 versus 113.5; 48–1,530) and total bilirubin concentration (0.5 mg/dL; 0.1–6.2 versus 0.25; 0–1.7) upon presentation, and their initial serum concentrations of albumin (2.9 g/dL; 1.4–4.1 versus 3.3; 2.2–3.9) were lower than those of survivors. Nadir serum albumin concentration was also lower in nonsurvivors (1.9; 1.4–3.7 versus 3.2; 1.8–3.5). A higher proportion of nonsurvivors had prolonged coagulation times, prothrombin time. and partial thromboplastin time. In a multivariate model, administration of charcoal at initial presentation was associated with longer survival (heart rate [HR] 0.019, 95% CI 0.001–0.644), while high serum aspartate aminotransferase activity was a negative prognostic factor (HR 118.2, 95% CI 2.89–4,826).

Conclusions and Clinical Importance: Cycad intoxication is associated with a higher case fatality than previously published. Several laboratory parameters might help differentiating potential nonsurvivors from survivors. Administration of charcoal as part of the emergency treatment appears to have a protective effect.

Key words: Acute liver failure; Hepatic toxicosis; Sago palm.

Cycad palms, also called Sago palms, are common in many parts of the world. In the United States, the term 'cycads' most commonly refers to the species *Cycas revoluta*, *Cycas circinalis*, and *Zamia floridana*. They are part of the native flora in tropical and subtropical regions, and are popular ornamental plants used in landscaping in the southern United States and Hawaii.[1] As houseplants and bonsai, these plants are becoming more common in the northern United States.[2] Cycads have been used in folk medicine and as a food source in many cultures, and toxicity of the plants has long been known.[3] Important toxins include cycasin, β-methylamino-L-alanine, and an unidentified high molecular weight compound.[4] The last 2 are neurotoxins; however, the unidentified compound is thought to be responsible for clinically observed neurologic signs. These toxins can be found in all parts of the plant, but seem to be present in highest concentration in the seeds and roots.[5]

After ingestion the predominant toxin, cycasin, is metabolized by the intestinal flora to its active compound, methylazoxymethanol (MAM). This is a neurotoxic, carcinogenic, mutagenic, teratogenic, and hepatotoxic compound.[4,6–9] Carcinogenicity has been well demonstrated in rats[10] and nonhuman primates.[11] No link has been found between colon cancer and cycasin consumption in humans; however, cycasin's unique metabolism has made it useful as a model in rats.[12,13] In humans, Guam neurodegenerative disease, defined clinically by amyotrophic lateral sclerosis, Parkinsonism-dementia complex (PDC), dementia alone, or combinations (ALS/PDC), has been correlated with the concentration of cycasin in traditional foods.[9,14] In domestic ruminants, cycad intoxication results in 2 distinct syndromes. Acute intoxication results in gastrointestinal and hepatic toxicoses, and is more common in sheep. Chronic exposure causes a neurologic syndrome, most often seen in cattle. Neurologic signs are highlighted by a progressive and irreversible posterior paralysis, a condition commonly called "rickets," "wobbles," or "zamia staggers."[3,4,6,7,12,15]

Toxicosis in dogs is characterized by gastrointestinal and hepatic disease caused by MAM.[5,7] Cycasin is found in highest concentrations in the seeds, but is present in all parts of the plant.[5] The first publication reported cycad intoxication in 2 dogs resulting in acute gastrointestinal

Abbreviations:

ALP	alkaline phosphatase activity
ALS	amyotrophic lateral sclerosis
ALT	alanine transaminase
AST	aspartate aminotransferase
LSU VTH&C	Louisiana State University Veterinary Teaching Hospital and Clinics
MAM	methylazoxymethanol
PDC	Parkinsonism-dementia complex
PT	prothrombin time
PTT	partial thromboplastin time

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and hepatic signs with subsequent coagulopathy. One dog died 6 days after exposure, and the other was euthanized 10 days after exposure attributable to severe disease.[6] Another paper described 3 Bull Terriers which demonstrated acute gastrointestinal signs and liver insult. All 3 dogs recovered uneventfully.[8] Finally, a retrospective study evaluated 60 cases reported to the National Animal Poison Control Center from January 1987 to November 1997. In this group, 95% developed gastrointestinal tract problems and 53.3% exhibited neurologic signs. The mortality rate was 32%; however, ingestion of cycad plant material was only documented in 27% of the cases.[16] The present retrospective study was undertaken to reassess the outcome of cycad intoxication in dogs with documented intoxication. Another goal was to identify possible prognostic factors in a cohort of affected dogs.

Materials and Methods

Criteria for Case Selection

Medical records of the Louisiana State University Veterinary Teaching Hospital and Clinics (LSU VTH&C) were searched to identify dogs with a diagnosis of documented or suspected cycad palm ingestion. Records of dogs seen over a 7-year period (September 2003 to August 2010) were searched. Fifty-nine medical records from dogs presented because of cycad intoxication were retrieved. Dogs were classified as documented ingestion if the owner reported exposure or if cycad plant material was evident in the vomitus or stool. Only dogs with documented ingestion of cycads were included in this study.

Data Collection

The following historical data were collected when available: signalment, body weight, presenting complaint, time from ingestion to presentation, clinical signs, and time of onset of clinical signs before presentation. Physical examination data collected included habitus, temperature, pulse, respiration rate, hydration status, and any pertinent physical examination findings. Results from the following diagnostic procedures were reviewed when available: packed cell volume and concentration of total solids, blood glucose and blood lactate, bile acids, fibrinogen, complete blood count, biochemistry panel, urinalysis, prothrombin time (PT), partial thromboplastin time (PTT), colloid osmolality, abdominal radiographs, abdominal ultrasound, liver biopsy, and necropsy findings. Presenting and serial laboratory values were reviewed. Blood lactate was determined with hand-held analyzers upon admission into the intensive care unit.[a] PT and PTT were often performed cage side during after-hours emergency.[b] Otherwise all testing was performed in the LSU VTH&C Clinical Pathology laboratory. The medical therapy was also reviewed in each case. Outcome was determined by reviewing the medical records and calling clients and referring veterinarians for updates as of August 2010 as necessary. The cause of death was also recorded to differentiate animals that died from those that were euthanized. Additionally, reason for euthanasia was also noted when available.

Statistical Analysis

Depending on the outcome, cases were assigned either to the surviving or the nonsurviving group. Because of varying availability of data, and the goal of finding clinically useful prognostic indicators, statistical analysis of data focused on information obtained at initial presentation to the LSU VTH&C. In addition, the lowest serum albumin concentration obtained during the hospital stay was recorded to offset the possible effect of clinical or subclinical dehydration at the time of presentation. Variables recorded at the time of presentation, and the lowest serum albumin concentration, were compared between groups by the Wilcoxon rank-sum test for continuous data or the Fisher exact test for categorical variables with statistical significance set at $P < .05$. Additionally, all variables recorded at the time of initial presentation were evaluated as possible prognostic indicators (referral, presentation within 8 hours of ingestion, presentation within 12 hours of ingestion, presentation within 36 hours of ingestion, charcoal administration, blood lactate, serum aspartate aminotransferase [AST], alanine transaminase [ALT], alkaline phosphatase activity [ALP], total bilirubin, glucose, albumin, cholesterol, blood urea nitrogen, lowest serum albumin recorded during hospital stay, platelet count, increases in PT and PTT) by a univariate Cox proportional hazards model and those significant at a $P < .15$ were selected for a multivariate model allowing for interaction between variables. Multivariate analysis was performed with a forward stepwise selection. A $P < .05$ in the hazard ratio indicated statistical significance. Schoenfeld residual plots were evaluated graphically to test compliance with the proportional hazard assumption. All statistical tests were performed by commercial software packages.[c,d]

Results

Thirty-six dogs were identified with documented cycad palm ingestion. Two were lost to follow-up, and therefore were excluded from the study. Most dogs were presented with acute gastrointestinal signs, and showed evidence of hepatic insult (ie, increased liver enzymes) on serum chemistry. Most clients confirmed ingestion of cycad plant material by their pet, and ruled out exposure to other possible hepatotoxins. In the cases without witnessed ingestion, Sago palm plant material was observed in the vomitus or feces by the attending veterinarian. Dogs in this study ranged in age from 3 months to 10 years, with a median age of 1.5 years. Breeds included in this study were 7 mix breed dogs, 6 Labrador Retrievers, 3 Chihuahuas, 2 each of Pug, Yorkshire Terrier, Doberman Pinscher, Golden Retriever, Dachshund, Pomeranian, and 1 each of West Highland White Terrier, Miniature Schnauzer, Miniature Pinscher, American Eskimo, Great Dane, and Maltese. The median weight in kilograms of all dogs was 11.1, with a range of 1.8–56.6. For survivors, the median was 5.16 kg (range 1.8–56.6), and for nonsurvivors 20 kg (range 3–41) but this difference was not significant ($P = .07$). There were 14 males (12 neutered) and 20 females (10 spayed). When compared with all cases presenting to the LSU VTH&C over that time period, it was found that Dobermans and Pugs were overrepresented in the cycad palm toxicosis group.

Most dogs were examined in the spring and summer months, with 29 (85%) admitted between March and August (Fig 1). Seventeen dogs (50%) were initially presented within 8 hours of the onset of clinical signs or ingestion, 21 dogs (62%) were presented within 12 hours, and 31 (91%) were presented within 36 hours. Two dogs were presented with no clinical signs immediately after owners witnessed exposure. Twenty-nine dogs (85%) had a history of vomiting, 23 (68%) were lethargic, 10 (29%)

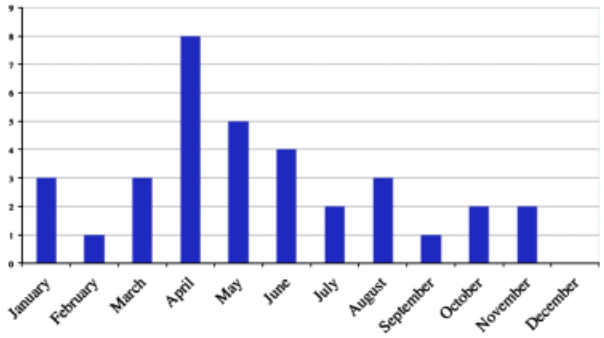


Fig 1. Number of cases presenting with cycad toxicosis per calendar month during the period of this study.

had diarrhea with 2 having melena or hematochezia, and 13 (38%) were reported to be anorexic. Fourteen dogs were referred by the primary veterinarian or an emergency facility. On initial physical examination, 6 dogs (17%) were hyperthermic (>102.5°F) and 1 was hypothermic (<99°F). Thirteen dogs (38%) were noted to be dehydrated, 5 (15%) had pale mucous membranes, and 2 were noticeably icteric. Three dogs were hypersalivating, 6 (17%) exhibited abdominal pain, 3 had distended abdomens, and 1 had petechiae present. Seven dogs (21%) had neurologic signs such as tremors, ataxia, mentation changes, and seizures. Two dogs developed subsequent pancreatitis during hospitalization. Length of hospitalization was not significantly different between survivors (median 3 days, range 0–14) and nonsurvivors (median 3 days, range 0–8). Most nonsurvivors were euthanized during their hospital stay (12/17, 70.6%), and 1 patient died. Four patients were euthanized 18, 29, 41, and 133 days, respectively, after discharge.

Initial laboratory abnormalities included mild hyperglycemia (141–164 mg/dL, reference range 100–130) in 6 dogs (of 32, 18%) and hypoglycemia (46–77 mg/dL) in 4 (of 32, 12%). Severe hypoglycemia (<60 mg/dL) occurred in 3 nonsurvivors, and none of the survivors. Six dogs (of 28, 21%) had a blood lactate concentration >2.5 mmol/L. On initial clinicopathologic data (available in 32 dogs), 19 dogs (59%) had increased AST (101–3,803 IU/L, reference range 0–50), 16 (50%) had increased ALT (124–4,123 IU/L, reference range 0–60), 11 (34%) had increased ALP (200–1,209 IU/L, reference range 0–100) activities in the serum, and 9 (28%) had an increased total bilirubin concentration (0.5–6.2 g/dL, reference range 0–0.3). Eight dogs (25%) were initially hypoalbuminemic (1.4–2.5 g/dL, reference range 2.6–4.2), and another 6 (total of 44%) became hypoalbuminemic (1.4–2.4 g/dL) at some point during hospitalization. Three dogs (9%) had an increased SUM (23–46 mg/dL, reference range 10–22), while 4 (12%) had decreased SUM concentration (5–9 mg/dL). No dogs had concurrent increases in serum creatinine concentration. Cholesterol analysis is not included in the after-hours chemistry panel and therefore was only performed for 13 dogs. Serum cholesterol concentration was decreased (77–111 mg/dL, reference range 150–240) in 8 dogs (61%) and increased in 2 (15%, 292 and 331 mg/dL). Ten dogs (34% of 29) had thrombocytopenia (24–216 × 10^9/L, reference range 220–600), which was severe in 3 (10%) dogs (<50 × 10^9/L), and moderate in 3 dogs (<100 × 10^9/L). One dog had a thrombocytosis (680 × 10^9/L). Both PT and PTT were prolonged in 13 of the 23 dogs evaluated (56%), with 2 dogs having only prolonged PTTs. Treatment varied depending on history and presentation. Nine dogs (26%) were given apomorphine to induce vomiting and 21 dogs (62%) were given activated charcoal as an intestinal adsorbent. Other treatments included fluid therapy, fresh frozen plasma transfusions, and administration of antibiotics, liver protectants, vitamin K_1, and lactulose.

Seventeen dogs (50%) died or were euthanized as a direct consequence of cycad intoxication. All survivors were reported to have made a full recovery with no known residual abnormalities. When the surviving and nonsurviving dogs were compared, 6 factors (initial ALT activity, initial serum albumin concentration, lowest recorded serum albumin concentration, and total bilirubin, increased initial PT, and increased initial PTT) were significantly different between both groups (Table 1). PT was increased in 9 of 11 tested nonsurvivors, and in 4 of 12 tested survivors (P = .025), while PTT was prolonged in 10 of 11 nonsurvivors and 5 of 12 survivors (P = .019). There was no significant difference in history or physical examination findings between surviving and nonsurviving dogs. This included time of presentation after ingestion and the presence of neurologic signs. The case fatality in the dogs that were referred cases was higher than primary cases (64% versus 40%), but this difference was not statistically significant (P = .14). Of the 21 dogs given activated charcoal, 13 survived. Only 4 survivors had not received charcoal. Only 1 surviving dog was hypoglycemic at presentation (77 mg/dL). Three dogs that died had severe hypoglycemia (<60 mg/dL).

Results of the univariate analysis identified variables with a P < .15, which were selected for the multivariate analysis. These variables were referral (P = .149), ingestion <8 hours before presentation (P = .128), charcoal administration (P = .035), serum glucose concentration (P = .007), log serum aspartate transaminase activity (P = .004), serum alanine aminotransferase activity (P = .004), total serum bilirubin concentration (P = .070), serum albumin concentration at presentation (P = .020), SUM (P = .056), platelet count (P = .038), prolonged PT (P = .022), and prolonged PTT (P = .041). In the multivariate model only charcoal administration (hazard ratio 0.019; 95% CI 0.001–0.644, P = .028) and log AST (hazard ratio 118; 95% CI 2.9–4,826, P = .012) were found to be significantly associated with outcome.

Histopathological data were reviewed from 5 dogs for which necropsy was performed. A range of changes was seen throughout the livers examined, but overall they fell into 3 categories consistent with acute, subacute, and chronic changes. The acute changes (0–2 days after ingestion) consisted primarily of centrilobular hemorrhage and congestion with moderate to marked centrilobular hepatocellular necrosis accompanied by variable amounts of neutrophilic infiltration (Fig 2). The subacute changes (23 and 28 days after ingestion)

Table 1. Median and range for quantifiable data compared between survivor and nonsurvivor groups.

	Survivors			Nonsurvivors		
	Number of Dogs	Median	Range	Number of Dogs	Median	Range
Age (years)	17	2	0.33–9	17	1.5	0.25–10
Weight (kg)	17	5.16	1.8–56.5	17	20	3.0–41
Lactate (mmol/L)	16	1.5	0.0–9.1	12	1.65	0.0–3.3
AST (U/L)	16	77	45–220	16	109.5	4.0–3808
ALT (U/L)	16	113.5*	48–1530	15	196*	16–4123
ALP (U/L)	16	142.5	31–988	16	192.5	63–1209
Total bilirubin	10	0.25*	0.0–1.7	13	0.5*	0.1–6.2
Glucose (mg/dL)	16	119	77–164	16	103.5	46–146
Albumin (g/dL)	16	3.3*	2.2–3.9	16	2.9*	1.4–4.1
Nadir albumin (g/dL)	13	3.2**	1.8–3.5	16	1.9**	1.4–3.7
Cholesterol (mg/dL)	5	114	80–292	8	129.5	77–331
BUN (mg/dL)	16	14	5.0–30	16	17	8.0–46
Platelets ($\times 10^9$/L)	15	223	237–680	14	187	24–564

All laboratory data were collected at presentation, other than the lowest albumin. Medians, ranges, and number of dogs are shown for continous data subjected to Wilcoxon rank test.

*Significantly different between both groups ($P < .05$).

**Significantly different between both groups ($P < .0005$).

were more substantial and consisted of severe centrilobular coagulative necrosis with widespread hepatocellular degeneration and scattered attempts at regeneration. Affected hepatocytes also tended to be swollen (hydropic degeneration). The most severe cases revealed stromal collapse with early periportal fibrosis and bile duct proliferation. All dogs had variable amounts of neutrophilic, lymphocytic, and plasmacytic infiltration. Occasional cases also had scattered extramedullary hematopoiesis (Figs 3 and 4). The chronic changes (41 and 53 days after ingestion) were typical of a longer time course, consisting of diffuse hepatocellular necrosis, degeneration and regeneration with extensive stromal collapse, bridging fibrosis with nodular regeneration, biliary hyperplasia, distended bile canaliculi, often with bile plugs, and lymphocytic and plasmacytic infiltration (Fig 5). One dog had acquired portosystemic shunts. When present, attempts at regeneration included prominent mitotic

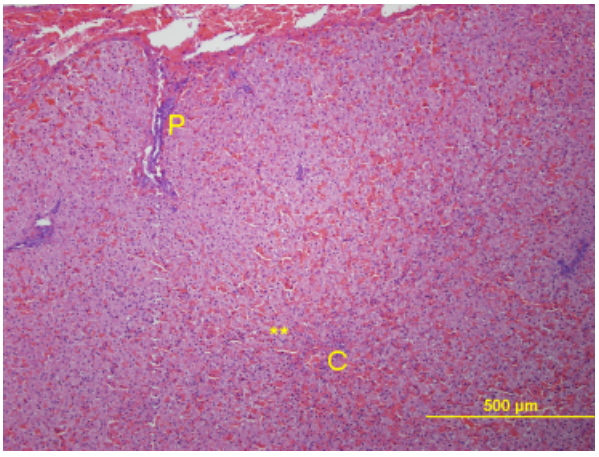
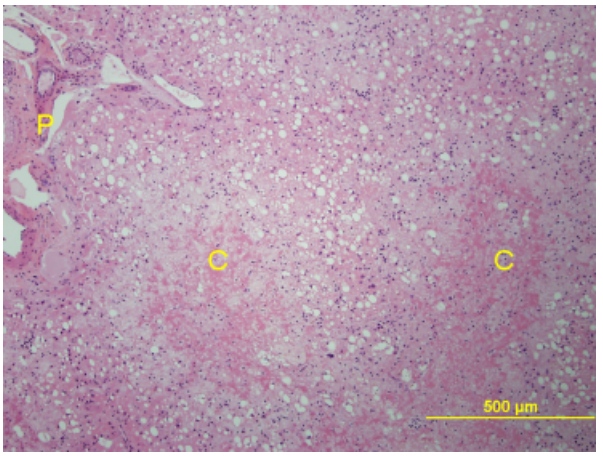


Fig 2. Example of acute changes in a dog that died as a result of cycad toxicosis. Centrilobular (C) and periportal (P) regions are congested and hemorrhagic with moderate hepatocellular necrosis and variable neutrophilic infiltration (**); liver, HE stain, 100×.



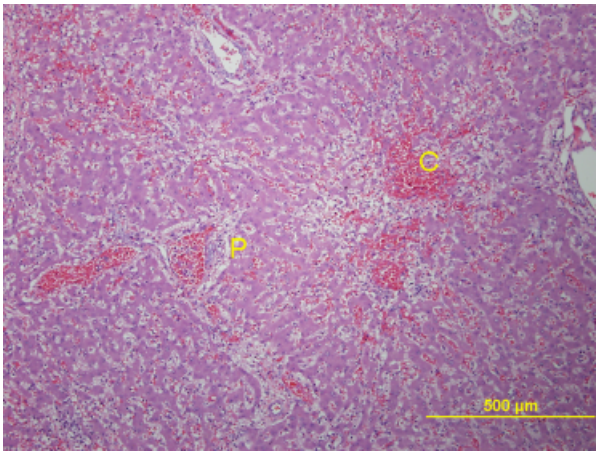


Fig 3 & 4. Examples of subacute changes in a dog that died as a result of cycad toxicosis. Centrilobular regions (C) exhibit moderate to marked coagulative necrosis with stromal collapse. There is widespread hepatocellular degeneration with attempts at regeneration and scattered neutrophilc, lymphocytic, and plasmacytic infiltration. Portal areas (P) are fibrotic with biliary proliferation; liver, HE stain, 100×.

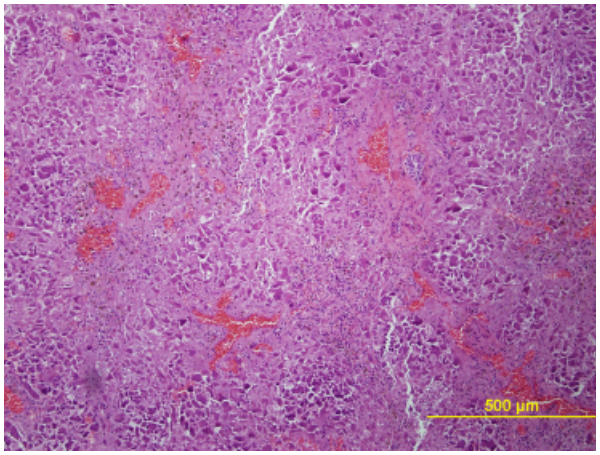


Fig 5. Histopathology from a case with chronic changes. There is diffuse hepatocellular necrosis, degeneration, and regeneration with extensive stromal collapse, bridging fibrosis with nodular regeneration, biliary hyperplasia, distended bile canaliculi, often with bile plugs, and lymphocytic and plasmacytic infiltration; liver, HE stain, 100×.

activity, megalocytosis, karyomegaly, and occasionally multinucleate hepatocytes.

Discussion

The goal of this retrospective study was to evaluate the outcome of cycad intoxication in dogs and identify factors associated with mortality that may aid the clinician with prognosis in an individual patient. Case fatality rate was 50%, a higher proportion than was previously reported (32.1%).[16] This difference in outcome might be explained by the fact that the previous retrospective study was based on data collected at a toxicology consultation center and not on actual medical records. Cases included in that report were classified as possible toxicoses, (13.3%), suspected toxicoses (60.1%), and toxicoses (26.6%). While dogs in the toxicoses group had documented ingestion, those in the 'suspect' group were defined as having a characteristic clinical syndrome with some data unavailable and animals with 'possible' toxicosis only had a few signs consistent with the syndrome. Data were reported for the group with no differentiation between the categories.[16] Therefore, it is possible that some survivors were not exposed to cycads, and this fact could have favorably influenced the case fatality rate. The cases in the present study were strictly limited to documented ingestions. The case fatality rate in the present study was consistent with anecdotal reports such as the press release[17] from the American Society for the Prevention of Cruelty to Animals Animal Poison control center, "Trouble in Paradise: Sago Palm", which stated that there has been an increase of >200% in cycad palm cases reported to the center over the past 5 years, with 50–75% ending in death.[17]

Because of the limited number of cases, and the varying availability of data, risk factors for death could not be determined in the previous study. Significant differences were found between the surviving and nonsurviving groups in our study, however, and they appear to be associated with serious complications of acute liver insult and necrosis, such as cholestasis, DIC, and sepsis.

Most dogs were presented in the spring and summer months (March through August). This could be associated with the time of year when people are likely to be out working in the yard. In addition, seeds often start falling from the plant between January and March and can continue to drop over 10–30 days.[1,18] Dobermans and Pugs appeared overrepresented among dogs with cycad palm toxicosis. The reason for this finding is unknown, and the small number of animals included in the study precludes any meaningful conclusion about breed predisposition. Most dogs presented within 12–36 hours of the onset of clinical signs, which most commonly included vomiting, lethargy, and diarrhea. Presentation was similar to previous reports, although neurologic signs were not as common.[6,8,16]

Activated charcoal administration had a protective effect in our study group. It is plausible that administering activated charcoal, an adsorbing agent, is beneficial to dogs that have ingested cycads or other toxins. There could be a bias, however, since charcoal is never administered to vomiting, unstable dogs. Therefore, administration of activated charcoal could select dogs with less severe disease and a potentially better outcome.

There was no significant difference in glucose between survivors and nonsurvivors; however, severe hypoglycemia only occurred in nonsurvivors (4 dogs < 60 mg/dL). Hypoglycemia could have been associated with liver failure, or sepsis. Signs of sepsis have been shown to adversely affect prognosis in humans with fulminant hepatic failure.[19,20] Total bilirubin concentration was found to be significantly higher in nonsurviving dogs. This likely represents cholestasis caused by disruption of bile production or flow after toxin exposure.[21,22] The difference between the median serum ALT activity was found to be statistically significant between survivors and nonsurvivors. However, the differences in the numerical data do not appear to be clinically significant, as the median serum activities of these enzymes would be categorized as mildly to moderately increased for both survivors and nonsurvivors. Therefore the clinical relevance is questionable. There was no significant difference in the SUM in nonsurvivors, with increases likely reflecting more severe dehydration or gastrointestinal bleeding in some dogs. Renal azotemia is unlikely caused by the lack of concurrent increase in creatinine. Decrease in serum albumin concentration upon presentation was a significant factor, as well as the difference in lowest recorded serum albumin concentration. Hypoalbuminemia could be a consequence of liver failure, but could be associated with gastrointestinal or urinary loss, or owing to leakage into body cavities or tissues associated with increased vascular permeability.

Eight dogs (of 10) with thrombocytopenia had abnormal coagulation tests (PT, PTT, or both). One thrombocytopenic dog did not have coagulation tests performed. Increases in PT and/or PTT were more frequently observed among nonsurviving dogs. Severe liver

insult leads to decreased synthesis of coagulation factors or synthesis of abnormal coagulation factors. In addition, disruption of enterohepatic circulation of bile acids can lead to decreased intestinal absorption of vitamin K, which can prevent activation of profactors and increase procoagulant proteins.[23] These coagulation abnormalities, especially with concurrent liver disease, gastrointestinal insult, or both, can lead to DIC, which could be the reason for thrombocytopenia seen in many of the nonsurviving dogs. Another potential cause for thrombocytopenia in these dogs could be loss, especially in those with severe gastrointestinal bleeding.[23]

Histopathologic changes were reported in one of the previous papers describing cycad toxicosis in dogs. In both dogs from that study the liver showed marked focal centrilobular and midzonal coagulation necrosis.[6] Centrilobular necrosis is the most common pattern of hepatotoxic injury and midzonal necrosis is the least common.[21,22] This is attributed to the high activity of mixed function oxidases in hepatocytes located near the central vein that are the most active in biotransformation of toxic substances. This pattern can also be seen with hypoxia, as anatomically this area is most distant from the hepatic arteries, or periportal area. Therefore, concurrent hypovolemia can worsen the cellular damage.[21,22] Although the lesions observed in the present cases are suggestive of cycad palm toxicosis, the cause of disease cannot be determined by morphology alone.[24]

The limitations of this study are those inherent to retrospective studies of small diverse clinical populations, where data have been collected in a clinical context. The retrospective nature also causes diversity in availability of information in medical records, diagnostic tests performed, conditions of testing, and treatment protocol. It would also be difficult to determine the effect of financial concerns on the decision to euthanize, as perceived prognosis in each particular case likely affected the clinician's discussion with the client. This study was limited to dogs with known exposure. It is likely that dogs with cycad ingestion were not all included in this study attributable to lack of clinical suspicion and available history. Larger, prospective studies on cycad toxicosis are required to provide detailed and robust data.

In conclusion, cycad intoxication can be associated with severe disease in dogs; the case fatality rate of dogs included in our cohort was higher than previously published. Several clinicopathologic parameters could be helpful in differentiating survivors from nonsurvivors on presentation. They likely reflect the severity of liver dysfunction, the presence of systemic inflammatory response syndrome, DIC, or a combination of these problems. Finally, administration of charcoal upon presentation was shown to be beneficial and should be attempted if the condition of the dog allows it.

Footnotes

[a] Lactate Pro, Arkray, KDK Corporation, Kyoto, Japan
[b] SCA2000, Veterinary Coagulation Analyzer, Synbiotics, San Diego, CA
[c] Number Cruncher Statistical Software, NCSS version 2001, break at Kays-ville, UT
[d] SAS 9.1, SAS Institute, Cary, NC

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