大韓獸醫學會誌(2007) 第47卷 第2號
Korean J Vet Res(2007) 47(2) : 209~212

Cycad revoluta toxicosis in a dog

Jong-Hyun Yoo, Hyuk-Tae Kim[1], Chul Park, Byeong-Teck Kang, Dong-In Jung, Eung-Je Woo[2], Hee-Myung Park*

College of Veterinary Medicine, Konkuk University, Seoul, 143-701, Korea
[1]Leesangyoon Animal Hospital, Seoul 140-853 Korea
[2]College of Electronics and Information, Kyunghee University, Gyeonggi-do 446-701, Korea
(Accepted: May 11, 2007)

Abstract : A 3-year-old female Cocker Spaniel dog acutely developed hepatopathy following ingestion of root of Cycad (*Cycas revoluta*). Seven hours after the ingestion, she showed acute continuous nausea, vomiting, and marked depression and was presented to the local veterinary clinic. At physical evaluation, the dog showed moderate weakness, pale mucous membrane, jaundice, and dehydration. Serum biochemical analysis revealed elevated alanine aminotransferase and aspartate aminotransferase, and mild azotemia. The dog was treated with intravenous fluid, antibiotics, and hepatic protectants for 10 days and recovered without any sequela. Although the ingestion of Cycad in dogs is rare, it can be treated successfully with appropriate supportive therapy.

Key words : acute hepatopathy, cycads, dogs, intoxication

Introduction

Cycads are members of ancient plant in the family Cycadacease and are found in tropical and subtropical regions over the world. *Cycas revoluta* is known as one of the popular ornamental and house plant in the northeastern Asia including Japan, China and Korea.

The toxic property of cycads has been described in various animals. Especially, cycads are hazardous to plant-eating domestic animal like cattle and sheep where the cycads are native [5, 6]. Cattle intoxicated with cycad shows ataxia in the hindlimb and characteristic gait, locally called “wobbles” or “rickets” due to axonal dystrophy in the spinal cords [7]. Cycad toxicosis is rarely reported in dogs with plant-eating behavior. Retrospective study in 60 dogs with evidence of cycad ingestion reveals that *Cycas revoluta* was the most commonly involved species and most dogs developed liver and gastrointestinal tract problems with recovery rate after treatment was 67.7% [1].

The object of this case report is to describe the clinical course of cycad intoxication in a dog and response to treatment. To the knowledge of author, this is the first case report of cycad intoxication in dogs in Korea.

Case Report

A 3-year-old female Cocker Spaniel dog acutely developed hepatopathy and gastrointestinal signs following ingestion of roots of *Cycas revoluta*. Six to seven hours after the ingestion, the dog had shown acute continuous nausea, vomiting, and marked depression and was presented to veterinary clinic. The owner notified that she had observed the dog eating several roots of cycad, which were also found in vomitus of dogs. At presentation, the dog showed moderate weakness, pale mucous membrane, and dehydration. At the first day of presentation, serum biochemical analysis revealed elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST), and mild azotemia (Table 1). Other clinicopathological findings including complete blood count (CBC) were within normal range. The dog was tentatively diagnosed as hepatopathy due to cycad intoxication and hospitalized for intensive care. The supportive treatment included fluid administration with 2.5% dextrose in 0.45% NaCl and activated charcoal at a dose of 1-2 g/kg BID at first day of presentation.

At the next day, severe icterus was detected (Fig. 1).

*Corresponding author: Hee-Myung PARK
College of Veterinary Medicine, Konkuk University, Seoul 143-701, Korea
[Tel: +82-2-450-3664, Fax: +82-2-450-3037, E-mail: parkhee@konkuk.ac.kr]

Table 1. Profiles of serum chemistry in a Cocker Spaniel dog intoxicated by cycad roots

	Day at presentation				
	1st day	2nd day	4th day	7th day	11th day
ALT (IU/l)	202	> 1500	> 1500	1390	660
AST (IU/l)	101	> 500	321	125	95.7
ALP (IU/l)	–	928	652	545	482
Total bilirubin (mg/dl)	–	4.6	> 12	3.0	1.31
BUN (mg/dl)	49	21	–	–	–
Creatinine (mg/dl)	0.4	0.5	–	–	–

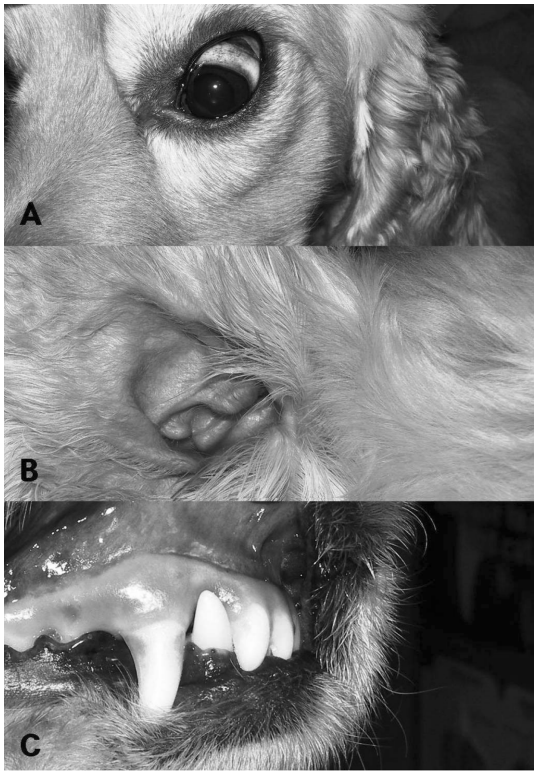

Fig 1. Icterus was observed in a female Cocker Spaniel dog a day after ingesting roots of cycad. Notable signs of icterus are seen in screla (A), inner pinna of ear (B), and gum and gingival regions (C).

Appetite was gradually improved. Vomiting was controlled spontaneously but retching was occasionally shown. Grossly, feces were normal. Laboratory value suggested severe damage of liver (Table 1). Supportive treatment included metronidazole (15 mg/kg, PO *bid*), Ranitidine (2.0 mg/kg, PO *bid*), Ursodeoxycholic acid (10 mg/kg, PO *bid*), L-glutathione (2.5 mg/kg, PO *bid*), and Biphenyl dimethyl dicarboxylate (Lepotil; Cellart Pharma, Korea) (0.25 mg/kg, PO *bid*) for 7 days. The dog was discharged at third day of presentation because she began to consume water by herself and activation was shown to be improved. However, since icterus was severe and hepatic profile of serum chemistry was in serious condition, the owner was requested for careful inspection and cares for the dog and feeding commercial veterinary prescription food (L/d; Hill's Pet Nutrition, USA). Then the dog was presented to the veterinary clinic every three days for the periodic monitoring of hepatic status. The hepatic profile of serum chemistry as gradually improved. Eleventh day after the presentation, icterus was resolved and the dog was clinically normal although serum hepatic enzyme level was still above the high range. The owner was recommended for the change of prescription diet to commercial canine diet. Since then, the owner has stopped to visit our hospital because she found that the dog was healthy. Follow-up call one month later found that she still maintained normal healthy state and activity without complications and, therefore, it was concluded that the dog was successfully recovered.

Discussion

Only a few reports have described the cycads intoxication in dogs [1, 2, 12]. The reason for unfrequent reports in dogs may be that the seed has unpleasant and strong tastes. In addition, acute vomiting due to the gastric irritation allows toxic materials to be eliminated, although not always enough, before massive absorption, which is most common clinical signs of cycad ingestion in dogs [1, 12]. Ingestion of all parts of cycads, including seed, stems, root, and leaves, has been reported to induce clinical signs in dogs [1, 2]. Our case of dog ingested several roots of cycads and showed acute signs of

intoxication. The exact reason for eating the roots in this case was unknown. Plant chewing and eating behavior is common in dogs and it may represent some kinds of self-remedy, needs for more fiber, play behavior, or attention-seeking [10].

Toxic ingredients of cycads, including azoxyglcosides (cycasin, neocycasins), macrozamin, and α-amino β-methyl diaminopropionic acid is known to contribute hepatotoxicosis and neurotoxicosis in animals [9, 11]. Cycasin is non-toxic to animal but it is converted to toxic metabolite, methylazoxymethanol by intestinal microflora. Methylazoxymethanol is metabolized to alkylating agents, leading to liver necrosis and fibrosis, gastrointestinal disease, and spinal cord damage with a degeneration of myelin in cattle [6, 8].

In dogs, liver is presumed to be the major target organ in cycads toxicosis [1, 12]. High levels of ALT, AST, and total bilirubin are often accompanied with fulminant hepatic failure and may be the primary cause of death in canine cycad toxicosis. Thus, careful monitoring the changes of hepatic enzyme and appropriate supportive therapy are recommended. The dog presented on here showed findings of severe hepatic damage, including icterus, markedly elevated hepatic enzymes. Icterus was found on the next day after cycad ingestion and had appeared up to 10th day. The levels of ALT and AST were acutely elevated at the 2nd day after ingestion which was consistent with findings reported in elsewhere [1]. Therefore, after tentative diagnosis of cycads ingestion, aggressive therapy is emphasized regardless of the relatively normal clinicopathological findings because of acute progression of the disease.

In addition, abnormal neurological signs, including weakness, ataxia, depression, proprioceptive deficits, and coma or seizures, have been also reported in 53.3% in cases of cycad toxicosis in dogs [1]. However, no report has described neurological signs related to spinal damage in dogs in contrast to those in cattle, sheep, and goats. In cattle and sheep, neurotoxicity of cycad palm induces significant lesions in both the central nervous system and the dorsal root ganglia of the spinal cords, which produce progressive, irreversible hind limb paralysis [6, 7]. However, pathological findings on nervous toxicity have been rarely reported in dogs. The dog in this case showed marked depression at first presentation. Neurological signs of hepatic encephalopathy, such as depression, ataxia, seizure activity, and coma, can also be secondary to fulminant hepatic failure [3]. Senior *et al.* [12] reported mild nerve fiber degeneration in cranial cerebella peduncle in a dog with generalized weakness, which suggest an association between obtunded mental signs and central nervous lesion due to cycasin intoxication.

Azotemia due to cycad intoxication was reported in a few dogs [12] and supposed to be secondary to hyperbilirubinuria and reduction in renal perfusion caused by vomiting and subsequent dehydration rather than a direct effect of the toxin. In this case, mild azotemia is observed and resolved after fluid therapy.

The treatment of this toxicosis is supportive and no effective antidotes are available [9]. Supportive care, including inducing emesis, administration of activated charcoal provide, is crucial for increasing survival chance by decreasing the absorption of the cycasin [11]. Supportive treatment includes intravenous fluid administration for dehydration, antiulcer medication (cimetidine, sucralfate), and diazepam for the control of seizure [1]. We initiated fluid therapy to correct the dehydration and stimulate bile flow. The dog became more active and regained some degree of appetite although generalized icterus was present. Clinical status had been progressively improved. The serum levels of ALT and AST were remained high level because those enzymes decrease over several days to 2 weeks after active hepatic damage terminated [15]. Oxidative stress are commonly involved with acute hepatic toxicosis and emphasize the intervention with antioxidants, such as zinc, S-adenosyl-L-methionine (SAMe), and alpha-tocopherol (vitamine E), although those were not used in this case [13, 14]. Biphenyl dimethyl dicarboxylate is synthetic derivative of a constituent from the traditional Chinese herb *Fructus Schizandrae* and widely used for chronic viral hepatitis B and C in Asia [4]. In Korea, it is commonly used as liver protectant in small animal practice, but exact efficacy for liver injury in dogs has not been elucidated.

Prognosis may depend on the amount of absorbed toxin, degree of aggressive therapy and proper supportive care. Therefore, imminent gastric evacuation is significant, and several administrations of activated charcoal are needed. Careful intestinal enema or irrigation may be tried when several hours passed after the exposure to cycad. A trial of antibiotics for several days after exposure would be probably helpful to

decrease intestinal microflora which convert cycasin to toxic metabolites and further evaluation is required. On the basis of the findings in this report, initial aggressive treatment and careful monitoring for the hepatopathy is important in cycad toxicosis in dogs.

Acknowledgments

This work was supported by the SRC/ERC Program of MOST/KOSEF (R11-2002-103).

References

1. **Albretsen JC, Khan SA, Richardson JA.** Cycad palm toxicosis in dogs: 60 cases (1987-1997). J Am Vet Med Assoc 1998, **213**, 99-101.
2. **Botha CJ, Naude TW, Swan GE, Ashton MM, van der Wateren JF.** Suspected cycad (*Cycas revoluta*) intoxication in dogs. J S Afr Vet Assoc 1991, **62**, 189-190.
3. **Dewey CW.** Encephalopathies: disorders of the brain. In: Dewey CW (ed.). A Practical Guide to Canine and Feline Neurology. pp. 99-178, Brackwell Publishing Professional, Ames, 2003.
4. **Gao M, Zhang J, Liu G.** Effect of diphenyl dimethyl bicarboxylate on concanavalin A-induced liver injury in mice. Liver Int 2005, **25**, 904-912.
5. **Hall WT.** Cycad (zamia) poisoning in Australia. Aust Vet J 1987, **64**, 149-151.
6. **Hooper PT.** Cycad poisoning in Australia-etiology and pathology. In: Keeler RF, van Kampen KR, James LF (eds.). Effects of Poisonous Plants on Livestock. pp. 337-347, Academic Press, New York, 1978.
7. **Hooper PT, Best SM, Campbell A.** Axonal dystrophy in the spinal cords of cattle consuming the cycad palm, Cycas media. Aust Vet J 1974, **50**, 146-149.
8. **MacLachlan NJ, Cullen JM.** Liver, biliary system and exocrine pancreas. In: Thomson RG, Carlton WW, McGavin MD (eds.). Thomson's Special Veterinary Pathology. 2nd ed. pp. 81-115, Mosby, St. Louis, 1995.
9. **Osweiler GD.** Plant-related toxicoses In: Toxicology. pp. 361-407, Lippincott Williams & Wilkins, Philadelphia, 1996.
10. **Overall KL.** Miscellaneous behavioral problems: emphasis on management. In: Clinical Behavioral Medicine for Small Animals. pp. 251-273, Mosby, St. louis, 1997.
11. **Plunkett SJ.** Emergency Procedures for the Small Animal Veterinarian. p. 492, Saunders, Philadelphia, 2001.
12. **Senior DF, Sundlof SF, Buergelt CD, Hines SA, O'Neil-Foil CS, Meyer DJ.** Cycad intoxication in the dog. J Am Anim Hosp Assoc 1985, **21**, 103-109.
13. **Scherk MA, Center SA.** Toxic, metabolic infectious and neoplastic liver diseases. In: Ettinger SJ, Feldman EC (eds.). Textbook of Veterinary Internal Medicine. 6th ed. pp. 1464-1478, Saunders, Philadelphia, 2005.
14. **Stehbens WE.** Oxidative stress, toxic hepatitis, and antioxidants with particular emphasis on zinc. Exp Mol Pathol 2003, **75**, 265-276.
15. **Willard MD, Twedt DC.** Gastrointestinal, pancreatic and hepatic disorders In: Willard MD, Tvedten H, Turnwald GH (eds.). Small Animal Clinical Diagnosis by Laboratory Methods. 3rd ed. pp. 172-207, Saunders, Philadelphia, 1999.