

Clinicopathological Analyses and Outcome of Acute Renal Failure with Grape Ingestion in Dogs

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(Accepted: February 15, 2013)

Abstract : Ingestion of grapes or raisins has been reported to the occurrence of acute renal failure (ARF) in dogs, although the mechanism remains undetermined. The prognosis often depends on the severity or clinical course of the disease at the time of presentation and is poor if the dog becomes anuric phase. To explore the characteristics and outcome of ARF caused by grape or raisin poisoning, sequentially collected data, from 2005 to 2008, of the Veterinary Medical Teaching Hospital at the Kangwon National University for clinical evaluation were retrospectively analyzed. Of the 11 clinically affected dogs, 4 cases made a full recovery, 3 died and 4 were euthanized. All but one case (raisin ingestion) had a history of grape exposure, but the exact quantity of fruit ingested was not known. The female dogs accounted for 72.7% (8 cases). Overall, the mean age was 5.3 years (range 0.2-11.3 years), and the mean body weight was 4.1 kg (range 1.4-13 kg). The average duration of hospital stay was 7.1 days (range 2-22 days). Vomiting and anorexia was reported in all dogs. Diarrhea (4 cases), oliguria (5 cases), and anuria (4 cases) with or without isosthenuria were also reported. Five dogs of 11 had mild to moderate anemia, with a decrease in packed cell volume and hemoglobin. All dogs had elevations in serum phosphorous, creatinine, and blood urea nitrogen values, but calcium values were variable; 2 dogs with hypocalcemia, 2 dogs with hypercalcemia, and the remaining 7 cases within reference interval. Dogs (n = 8) with measured on blood gas parameters had metabolic acidosis. In addition, higher serum enzyme activities were observed; amylase in 8 (72.7%) dogs, alkaline phosphatase in 7 (63.6%) dogs, and alanine aminotransferase in 5 (45.5%) dogs. Non-survived dogs revealed lower counts of platelet and lymphocyte subpopulation, as compared to the survived dogs.

Key words : acute renal failure, grape poisoning, dog.

Introduction

Since late 1980s, acute renal failure (ARF) presumably associated with ingestion of the fruits of *Vitis vinifera* (grapes, raisins, currants and sultanas) has been reported in dogs and is common emergency in veterinary medicine (1,2,3,5,8,9,11, 12,14). Clinical or pathologic signs reported included vomiting, anorexia, diarrhea, lethargy, and abdominal pain, increased blood urea nitrogen (BUN), creatinine, phosphorous, calcium, and serum osmolality (2,3,5,7,8,9,13,16). The exact mechanism of pathophysiology following grape or raisin ingestion has not been completely elucidated, although a variety of possible hypotheses including nephrotoxins leading to hypovolemic shock and renal ischemia (9), effects of tannins or high sugar consumption (10), mold toxins, contamination with pesticides or heavy metals (2,3) have been proposed. The purpose of this retrospective study was to characterize the diseases and clinicopathologic findings associated with ARF caused by ingestion of grapes or raisins in dogs that were

presented to Kangwon National University Veterinary Teaching Hospital (KNU).

Case

The clinical pathology database at KNU was searched to identify ARF in dogs, with a history of ingestion of grapes or raisins, referred to the VTH between 2005 and 2008. The following criteria were used to define ARF: (1) acute onset of clinical signs of ARF within the 7 days and history attributable to ARF (eg, vomiting, diarrhea, anorexia, oliguria, anuria, lethargy, and abdominal pain); (2) renal azotemia (serum creatinine concentration > 3.4 mg/dL and urine specific gravity < 1.025); and (3) normal to enlarged kidney size as detected by physical examination, radiography, or ultrasonography. Dogs with pre- and post-renal causes of azotemia were excluded from the study on the basis of clinical history, physical examination, clinicopathologic and radiographic findings, when available. Dogs with findings consistent with chronic renal failure were also ruled out. The following information was collected from the medical records: signalment (age, breed, and sex), body weight, serum total calcium, creatinine, BUN, phosphorous, albumin, total bilirubin, sodium, potassium,

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chloride, total carbon dioxide, blood pH, urine specific gravity, RBC count, hemoglobin, packed cell volume, mean corpuscular volume, mean corpuscular hemoglobin concentration, platelet count, WBC count, lymphocyte count, monocyte count, duration of hospitalization, time from ingestion of grapes or raisins to initial presentation and final outcome at 30 days after hospitalization. Because the medical records does not contain information concerning concurrent disorders, assessment of preexisting renal disease, heart disease, and previous exposure to nephrotoxicants including medications was not performed.

The primary endpoint was the death at 30 days after hospitalization. All laboratory test result measured at or during the first 24 hours of hospital admission was used, and continuous variables are presented as mean \pm standard deviation (SD) with the corresponding range. Established reference intervals were used to identify aforementioned clinicopathologic abnormalities.

Discussion

A total of 11 clinically affected dogs were identified, of which 10 dogs had a history of grape exposure with unknown quantity of fruit ingestion. Only 1 case was exposed to raisins. Breeds presented included Yorkshire terrier (n = 4), Shih tzu (n = 2), Maltese (n = 2), Cocker Spaniel (n = 1), Spitz (n = 1), and Pekingese (n = 1). Four cases made a full recovery, 3 died and 4 were euthanized; two of these were euthanized because of poor response to treatment and the other two cases were due to owner's economic reason. The 4 survived dogs were of mean (\pm SD) age 4.1 ± 2.1 years; 3 were female, mean body weight 3.8 ± 2.7 kg, time from ingestion of grapes or raisins to initial presentation 11 ± 1.5 , and the duration of hospital stay was 5.3 ± 1.3 days. The 3 non-survived dogs had a mean age of 6.5 ± 5.7 years, of which 2 were female. The mean body weight was 2.2 ± 0.4 kg, time from ingestion to the first presentation 22 ± 2.3 , and the mean length of hospitalization was 5.0 ± 2.6 days. All dogs had a

Table 1. Demographic and clinical characteristics of 11 acute renal failure cases at presentation

	Survived (n = 4)	Died (n = 3)	Euthanized (n = 4)
Age in years (Mean \pm SD, range)	4.1 ± 2.1 , 2.2-7.0	6.5 ± 5.7 , 0.2-11.3	5.9 ± 3.9 , 0.4-9.1
Male sex (%)	25.0	100.0	100.0
Weight in kg (Mean \pm SD, range)	3.8 ± 2.7 , 1.4-6.6	2.2 ± 0.4 , 1.7-2.4	5.7 ± 5.1 , 1.7-13.0
Vomiting, anorexia (%)	100.0	100.0	100.0
Diarrhea (%)	50.0	33.3	25.0
Oliguria (%)	75.0	33.3	25.0
Anuria (%)	25.0	66.7	25.0
Length of hospitalization in days (Mean \pm SD, range)	5.3 ± 1.3 , 4.0-7.0	5.0 ± 2.6 , 2.0-7.0	10.5 ± 9.3 , 2.0-22.0
Hours from exposure ¹ to admission (Mean \pm SD, range)	11 ± 1.5 , 12-48	22 ± 2.3 , 6-96	18 ± 4.7 , 6-96

¹Exposure represents to the ingestion of grapes or raisins. Of 11 affected dogs, 10 cases were associated with grape ingestion and 1 with raisin. Oliguria and anuria were based on the owner's report at initial presentation.

Table 2. Hematology results of 11 acute renal failure cases at presentation

	Survived (n = 4)		Died (n = 3)		Euthanized (n = 4)		Reference interval
	Mean \pm SD	Range	Mean \pm SD	Range	Mean \pm SD	Range	
Red blood cell count ($10^6/\mu\text{L}$)	4.6 ± 1.4	3.0-5.8	5.6 ± 0.7	5.0-6.3	4.2 ± 2.2	2.1-6.1	5.5-7.5
Hemoglobin (g/dl)	10.4 ± 3.2	6.5-13.0	10.7 ± 0.6	10.2-11.3	9.8 ± 4.9	5.0-14.4	12-18
Packed cell volume (%)	31.3 ± 10.3	20.2-40.9	43.7 ± 15.9	31.5-61.6	29.3 ± 14.7	15.2-42.6	37-55
MCV (fL)	67.7 ± 1.8	66-70	66.0 ± 3.0	63-69	70.7 ± 1.6	69.4-73.0	60-77
MCHC (%)	33.3 ± 2.0	31.7-36.1	32.2 ± 2.3	29.7-34.2	33.6 ± 0.7	33-34.4	33-36
Platelet ($10^3/\mu\text{L}$)	635.0 ± 317.5	332-990	116.7 ± 89.9	56.0-220	486.0 ± 142.3	305-606	200-500
White blood cell count ($10^6/\mu\text{L}$)	17.9 ± 10.6	11.1-33.7	16.5 ± 9.8	10.6-27.8	15.9 ± 5.6	8.0-20.5	6.0-17.0
Lymphocyte count ($10^3/\mu\text{L}$)	4.8 ± 5.9	0.6-8.9	1.0 ± 0.4	0.7-1.2	0.3 ± 0.1	0.2-0.4	1.0-5.0
Monocyte count ($10^3/\mu\text{L}$)	1.3 ± 1.6	0.2-2.5	0.9 ± 0.2	0.7-1.0	1.6 ± 1.5	0.5-2.7	0.2-1.3

Table 3. Serum biochemistry and urinalysis results of 11 acute renal failure cases at presentation

	Survived (n = 4)		Died (n = 3)		Euthanized (n = 4)		Reference interval
	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD	Range	
Blood urea nitrogen (mg/dl)	92.4 ± 36.4	57.6-130.0	107.0 ± 39.8	61.0-130.0	171.3 ± 136.5	87.0-374.0	7-28
Creatinine (mg/dl)	4.7 ± 2.0	2.0-6.4	8.7 ± 4.4	5.0-13.6	7.4 ± 3.3	3.2-11.1	0.9-1.7
Calcium (mg/dl)	10.0 ± 3.1	8.2-14.7	10.8 ± 2.5	8.4-13.4	7.4 ± 2.4	4.2-9.6	8.0-12.0
Phosphorous (mg/dl)	11.2 ± 4.1	7.8-16.1	15.3 ± 1.0	14.2-16.1	14.3 ± 3.2	10.6-16.1	2.8-6.1
Ca*P ^a	106.1 ± 26.9	69.5-133.6	163.7 ± 29.6	131.9-190.3	123.3 ± 42.2	75.3-154.6	< 70
Albumin (mg/dl)	3.2 ± 0.4	2.9-3.7	NA		2.8 ± 0.7	2.1-3.6	2.7-4.0
Total bilirubin (mg/dl)	0.4 ± 1.1	0.3-0.5	0.3 ± 0.1	0.2-0.4	0.3 ± 0.2	0.1-0.6	0-0.4
Sodium (mmol/L)	142.8 ± 16.2	120-158	149.3 ± 8.5	141-158	159.0 ± 7.5	152-166	145-155
Potassium (mmol/L)	4.6 ± 1.7	3.3-6.9	5.8 ± 2.8	3.2-8.8	5.4 ± 0.6	4.8-6.3	4.1-5.5
Chloride (mmol/L)	96.8 ± 20.1	73-122	103.7 ± 5.1	98-108	111.8 ± 7.4	105-120	100-120
Blood pH	7.241 ± 0.006	7.236-7.245	NA		7.187 ± 0.130	7.058-7.317	7.35-7.45
Total carbon dioxide (mmol/L)	13.5 ± 0.7	13.0-14.0	NA		13.3 ± 3.5	10.0-17.0	14-27
Urine specific gravity	1.010 ± 0.007	1.005- 1.020	NA		1.010 ± 0.005	1.005- 1.015	
Urine pH	5.8 ± 0.8	5.0-6.5	NA		6.2 ± 1.0	5.0-7.0	

^aSerum calcium times serum phosphorous product. NA = value not available.

sign of vomiting and anorexia. Also, diarrhea (4 cases), oliguria (5 cases), and anuria (4 cases) with or without isosthenuria were also observed.

Five dogs of 11 had normocytic, normochromic anemia when assessing with the packed cell volume and hemoglobin concentration; survived in 2 dogs, non-survived in 1, and euthanized in 2. The platelet counts were higher in survived dogs. The results of the leukocyte series were unremarkable with the exception of lower number of lymphocytes in non-survived dogs, when compared to the survived dogs. The evaluation of biochemical parameters revealed that all dogs had elevations in serum phosphorous, creatinine, and blood urea nitrogen values. However, the serum calcium concentrations after correcting for the albumin value were case-dependent; 2 dogs with hypocalcemia, 2 dogs with hypercalcemia, and the remaining 7 cases within reference range. Eight dogs with measured on blood gas parameters had a metabolic acidosis, as assessed with carbon dioxide and blood pH. Higher serum enzyme activities of amylase, alkaline phosphatase, and alanine aminotransferase were also observed in 8 (72.7%) dogs, 7 (63.6%) dogs, and in 5 (45.5%) dogs, respectively.

From the literatures (8,13), the dose ingested does not seem to be related to the severity of clinical signs or outcome. This may indicate that the ingestion of grapes or raisins, even a small amount, can cause lethal damage to the kidneys (4,6). Thus, early detection is critical for patients to facilitate full recovery (15). Although definitive cause-and-effect relationship between the dose ingested and onset of clinical signs has been identified in the documented cases, questions remain concerning raisin and grape toxicity, including the exact toxic principle as well as the mechanism of action responsible for

the toxicity. Further investigation on this subject is needed.

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개에서 포도중독에 의한 급성신부전의 임상병리학적 평가

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요 약 : 개에서 포도중독에 의한 신부전 치료결과에 대한 임상적 분석을 위하여 205-2008년 기간 중 강원대학교 수의과대학 동물병원에 내원한 환자의 의료기록부를 분석하였다. 총 11두 (암컷 8두) 중 4두는 완전히 회복하였고, 3두는 폐사, 4두는 안락사로 처리되었다. 1두를 제외한 모든 환자는 포도를 섭취하였으나 정확한 섭취량은 알 수 없었다. 환자의 평균 연령은 5.3세 (범위 0.2-11.3세), 체중은 4.1 kg (범위 1.4-13 kg)였으며, 평균 입원기간은 7.1일 (범위 2-22일)로 나타났다. 모든 환자에서 구토와 식욕부진 증상을 보였으며, 일부 환자는 설사 (4두), 췌노 (5두), 무뇨 (4두) 소견을 보였다. 모든 환자에서 혈청 phosphorous, creatinine, BUN 농도가 증가된 소견을 보였으며, 고칼슘혈증 2두, 저칼슘혈증 2두, 나머지 7두는 정상소견이었다. 혈청 농도가 증가한 항목은 amylase 8두, ALP 7두, ALT 5두였으며, 혈액 가스 분석에서 8두는 대사성산증을 보였다. 경미하거나 중등도의 빈혈 소견이 5두에서 관찰되었으며, 회복한 환자과 비교할 때 폐사축의 경우 혈소판과 림프구 수가 상대적으로 낮았다.

주요어 : 급성신부전, 포도중독, 개