



NOTE

Internal Medicine

Acquired Fanconi syndrome in two dogs following long-term consumption of pet jerky treats in Japan: case report

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ABSTRACT. Renal Fanconi syndrome has recently been associated with the ingestion of pet jerky treats from China in mostly small breed dogs in North America, Australia and Europe. We report here about two dogs with Fanconi syndrome following pet jerky treats exposure in Japan. A mixed-breed dog and a French bulldog showed weight loss, polyuria and polydipsia. For years, the owners had been feeding large quantities of pet jerky treats containing chicken prepared in China. Diagnostics revealed glycosuria without hyperglycemia, severe aminoaciduria, and in one case also ketonuria, hypokalemia and metabolic acidosis. A diagnosis of Fanconi syndrome associated with long-term consumption of Chinese pet jerky treats was made. Both dogs recovered fully following withdrawal of the pet jerky treats and supportive care. Fanconi syndrome of dogs in association with the consumption of pet jerky treats of Chinese origin can cause a broad proximal tubular defect with glycosuria and generalized amino aciduria, and should be also considered in Asia. Jerky treats associated Fanconi syndrome can be completely reversible following withdrawal of the treats and supportive care to correct the metabolic abnormalities.

KEY WORDS: Fanconi syndrome, glycosuria/glucosuria, jerky treats, kidney, renal tubular defect

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Renal Fanconi syndrome is associated with multiple defects of the proximal tubules. It causes impairment of reabsorption of molecules, such as glucose, amino acids and bicarbonate in the nephrons of the proximal tubules, eventually leading to renal tubular acidosis and renal failure. In dogs, Fanconi syndrome is well known as a familial disease in Basenjis [13]. Acquired renal Fanconi syndrome is caused by several drugs such as gentamicin, tetracycline and azathioprine, exposure to toxins such as heavy metals, infections such as leptospirosis [6–8] and certain diseases such as primary hypoparathyroidism and copper associated hepatopathy [2, 5, 9].

Fanconi syndrome has also been associated with ingestion of pet jerky treats mostly produced in and/or sourced from China [1, 3, 4, 6–9, 12, 15]. Toy or small breed dogs, such as the Chihuahua, Maltese, Yorkshire, Jack Russell and West Highland White Terriers are more predisposed likely, because of the higher proportion of jerky treats consumption to body weight [6–8]. The brachycephalic breeds, except for the Shi Tzu, seem to have a lower risk possibly because of their inability to chew jerky treats [8]. Jerky treats associated Fanconi syndrome has originally been reported from North America [1, 6–8] and Australia [15], and only recently from Europe [3, 4, 10, 12]. A single Jack Russel Terrier with pet jerky treats associated Fanconi syndrome has most recently been described from Japan [11], and here, we report on two other cases following long-term consumption of pet jerky treats.

Case 1. A 4-year-old spayed female mixed-breed dog, weighing 11.6 kg (BCS, body condition score 2/5), was presented to the Veterinary Teaching Hospital (KUVTH), Kagoshima University, Kagoshima, Japan, with a 15-day history of inappetence, vomiting, weight loss, lethargy, dehydration, polyuria and polydipsia. The dog had failed to improve with fluid and antibiotic therapy by the primary care clinician. Physical examination findings were unremarkable. Abnormal results of routine blood tests included moderate thrombocytopenia ($76 \times 10^9/l$; reference range, $211\text{--}621 \times 10^9$), hypokalemia (2.1 mmol/l; 3.9–5.1), hypocalcemia (2.1 mmol/l; 2.3–2.9), hypophosphatemia (0.5 mmol/l; 0.9–1.7) and increased serum alkaline phosphatase (1,357 U/l; 1–114) and alanine aminotransferase (124 U/l; 10–109) activities. Concentrations of blood urea nitrogen (4.6 mmol/l; 2.9–10),

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Table 1. Urinary amino acid analysis in dogs exposed to pet jerky treats and following withdrawals

Amino acid	Concentration ($\mu\text{mol}/\text{mg}$ urinary creatinine)						
	Control ^{a)}	Case 1		Case 2			
		1-wk	13-wk	4-wk	12-wk	20-wk	24-wk
Asparatic acid	1	6	8	21	0	17	0
Threonine	34	1,930	32	1,961	1,479	352	202
Serine	227	2,625	116	707	1,158	252	139
Asparagine	61	893	42	274	289	94	43
Glutamic acid	119	156	23	253	245	80	25
Glutamine	134	7,090	72	3,483	2,999	1,211	423
Proline	NA	283	NA	233	374	76	52
Glycine	108	12,978	81	963	1,427	513	232
Alanine	169	4,801	138	954	1,971	389	262
Valine	70	316	7	73	66	20	7
Cystine	132	78	22	527	283	199	54
Methionine	2	143	NA	19	NA	27	NA
Isoleucine	9	160	NA	26	39	11	NA
Leucine	7	394	NA	0	66	32	NA
Tyrosine	18	213	NA	138	196	38	NA
Phenylalanine	23	151	8	39	58	16	7
Histidine	16	1,199	21	306	399	96	57
Tryptophane	5	86	18	61	NA	18	NA
Lysine	46	249	NA	555	311	163	93
Arginine	37	10	14	347	174	90	46
Total	1,217	33,852	601	10,938	11,532	3,692	1,641

a) Mean value of the amino acid concentrations of three healthy dogs, wk: week after first presentation, NA: not assigned.

creatinine (97.3 mmol/l; 44.2–150) and glucose (4.4 mmol/l; 4.3–6.6), and other routine test results were all within normal reference ranges. Venous blood gas analysis revealed metabolic acidosis with a pH of 7.23 (7.36–7.44), total CO₂ concentration of 16.0 mmol/l (25–27), bicarbonate concentration of 14.7 mmol/l (20–29) and base excess of –13 mmol/l (–4–4).

Urinalysis showed glycosuria (4+), ketonuria (2+), pH 5.0, specific gravity of 1.023 (despite the animal being mildly dehydrated) and many epithelial cells and granular casts. The urinary protein/creatinine ratio was within the normal range (0.15; normal range <0.5). Urine culture was negative for bacterial growth.

Considering these test results, Fanconi syndrome was suspected. Quantitative urinary amino acid analysis (SRL, Tokyo, Japan) revealed severe generalized aminoaciduria (Table 1) further supporting the diagnosis of Fanconi syndrome. Upon further inquiries, the owner reported the dog being addicted to jerky treats 3 times a day (1 or 2 pieces at a time) for a few years. Most of treats contained chicken products and originated from China. The owner was instructed to completely withdraw any jerky treats and start feeding a balanced high quality diet by the clinician at the KUVTH. Furthermore, the electrolyte and blood gas abnormalities were corrected by the primary care clinician. Clinical signs resolved quickly within a couple of days, while glycosuria (3+) persisted for at least a week, but all laboratory test results were normal after 13 weeks including the urine amino acid pattern (Table 1).

Case 2. A 6-year-old intact male French bulldog, weighing 15.6 kg (BCS 2/5), was referred to the KUVTH, for glycosuria without hyperglycemia. The owner reported weight loss, polyuria and polydipsia. Physical examination findings were unremarkable. The findings of complete blood count and venous blood gas and serum chemistry analyses were also unremarkable. Urinalysis revealed glycosuria (2+), isosthenuria (specific gravity of 1.009) and aciduria (pH of 7.0). The urinary protein/creatinine ratio was at the upper limit of normal (0.5), and many epithelial cells and granular casts were noted.

After 4 weeks, glycosuria (3+), isosthenuria (specific gravity of 1.015) and aciduria (pH of 6.0) were remained unresolved, and urinary amino acid analysis (SRL) revealed severe generalized amino acids (Table 1), leading to the diagnosis of Fanconi syndrome. Upon further inquiries, the owner reported that the dog was consuming pet jerky treats, many of them contained Chinese chicken products, almost daily 4 times a day (1 or 2 pieces at a time) for the past 5 years. The owner was instructed to completely withdraw any treats at the first presentation. The results of urinary amino acid analyses after 12, 20 and 24 weeks revealed a gradual resolution of amino aciduria (Table 1). The results of urinary dipstick tests revealed mild glycosuria (1+ or \pm) at 12 and 20 weeks and resolution of glycosuria (–) 24 weeks after the first presentation.

Renal Fanconi syndrome should be considered when seeing a dog with glycosuria and normoglycemia. The association between Fanconi syndrome and ingestion of pet jerky treats produced in China and/or containing Chinese ingredients (chicken, duck and even vegetables) has received much attention in recent times [6–8]. In the present report, neither of the dogs had been exposed to any possible causes of acquired Fanconi syndrome other than pet jerky treats and experienced no other illness in the distant or recent past. The owners of the cases presented here reported feeding several times daily chicken jerky treats made in China for years. It remains unclear why the clinical signs and Fanconi syndrome were only evident after years of exposure, but may be

related to a more recently fed toxic jerky product.

In addition, clinical signs and laboratory test abnormalities were completely reversible after withdrawal of the treats in both cases, lending further support that the consumption of jerky treats caused Fanconi syndrome in the cases reported here from Japan. The specific constituents of jerky treats that cause Fanconi syndrome in dogs are yet to be identified. In survey by the US Food and Drug Administration and other institutions, minor adulteration with varied antibiotics and other chemicals were detected in the poultry jerky treats [14, 16], but there was no evidence that these contaminants are responsible for Fanconi syndrome in dogs.

Fanconi syndrome associated with the consumption of jerky treats is more frequently seen in small breed dogs [6–8, 15]. This predisposition might be related to the proportionally larger quantities of treats ingested by smaller breeds compared to that ingested by large dogs, or it may reflect a greater hypersensitivity of small breed dogs to the constituents of jerky treats compared to that of larger dogs [6–8]. In the present report, both of the affected dogs were of medium-sized, but they were addicted to jerky treats for years. Therefore, even medium-sized breed dogs may experience Fanconi syndrome when fed larger quantities and possibly over a long-time period.

Brachycephalic dogs are known to exhibit low susceptibility for Fanconi syndrome associated with the consumption of jerky treats [8]. However, in this report, we encountered a case of a French bulldog, which is a brachycephalic breed, affected by Fanconi syndrome. Again, this may have occurred because this French bulldog received large quantities of jerky treat daily for years.

In this report, the time to recovery time after discontinuation of jerky treats differed between the two cases. This may be due to the different degrees of the proximal tubular defect in each dog, which was probably caused by a difference in factors, such as the amount of intake, period of exposure to toxic constituents, individual susceptibility, age and breed. Additionally, the concentrations of urinary amino acids and their pattern differed between the two cases. This difference may reflect the severity of the tubular defect. These questions could be answered by the analysis of more cases in the near future. Therefore, a further study is required on Fanconi syndrome that is associated with jerky treats.

Fanconi syndrome as well as gastrointestinal disturbances associated with the consumption of jerky treats in dogs has been commonly encountered (>1,000 dogs) in North America [1, 6–8] and Australia [15] and only recently in Europe [3, 4, 10]. Japan is a non-epidemic country, and beside this report, there was only one small breed dog with jerky treats associated Fanconi syndrome described [11]. It is unclear why this problem has not been noted in Japan and China as Chinese pet jerky treats are also fed to dogs in Asia. It is unlikely that these jerky treats are produced by different manufacturers for Asia versus other parts of the world. Also, it appears that pet owners in Japan are having similar opportunities to purchase these Chinese pet jerky treats and also like to feed them just like in other countries. Maybe, these initial cases from Japan will alert the Asian veterinarians to this intoxication and caution owners of pets of feeding pet jerk treats until the specific cause has been identified and removed from these products.

In conclusion, two cases of canine Fanconi syndrome following ingestion of Chinese pet jerky treats were reported from Japan. This illness has become a serious health issue in dogs in North America, Australia and Europe; however, few cases have been reported in Asia. Asian veterinarians and pet owners should take careful precautions and be aware of the health-related issues resulting from the consumption of Chinese pet jerky treats.

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