pISSN 1598-298X
J Vet Clin 31(6) : 535-538 (2014)

Journal of Veterinary Clinics
www.ksvc.or.kr

Renal Amyloidosis in a Beagle

Joohyun Jung, Jaebong Jin, Hyunuk Lee and Mincheol Choi*[1]

Ilsan animal medical center, Daehwa-dong 2030, Ilsanseo-gu, Goyang-si, Gyeonggi-do 411-803, South Korea
**Veterinary Radiology Department, College of Veterinary Medicine and*
Research Institute for Veterinary Science, Seoul National University, Seoul 151-742, South Korea

(Accepted: December 16, 2014)

Abstract : An eight-year-old intact male Beagle had anorexia, vomiting, depression for two days. The dog had hypoalbuminenia and mild azotemia on hematologic and clinical chemistry examinations. Severe proteinuria was identified on urinalysis. On abdominal ultrasonographs, there were small amount of ascites and bilateral renomegaly with severe hyperechoic renal cortex and hyperechoic medullary rim sign. Renal biopsy and histopathology revealed renal amyloidosis. The quality of life in this dog was satisfactory with aggressive supportive care for three months. Euthanasia was performed due to deteriorated azotemia and nephrotic syndrome.

Key words **:** Amyloidosis, beagle, biopsy, renal.

Introduction

Renal amyloidosis is one of glomerular diseases characterized by extracellular amyloid infiltration and lead to life threatening organ failure. Kidney is the most common organ with amyloid infiltration in dogs and cats (19,20,21). This case describes diagnosis and medical management of renal amyloidosis in a Beagle dog.

Case

An eight-year-old intact male Beagle had a history of depression, anorexia, and vomiting for two days. There were no significant findings on physical examination. The hematologic and clinical chemistry works showed decreased albumin level of 1.2 g/dl (normal: 2.9~4.2 g/dl) and calcium level of 8.1 mg/dl (normal: 9.3~12.1 mg/dl). And there were increased blood urea nitrogen (BUN) level of 68 mg/dl (normal: 8~26 mg/dl), creatinine level of 1.9 mg/dl (normal: 0.5~1.3 mg/dl), and phosphorus level of 6.3 mg/dl (normal: 3~6.2 mg/dl). All other clinical blood values including baseline serum cortisol were within normal limits. Urinalysis showed normal urine specific gravity of 1.029 (normal: 1.015 to 1.040) but severe proteinuria with urine protein/creatinine ratio (UPC) level of > 20 (normal: < 0.5 when azotemia). There was mild serosal detail loss on the abdominal radiographs. On abdominal ultrasonographs, small amount of anechoic ascites was found. There were mild renomegaly with severe hyperechoic renal cortex and hyperechoic medullary rim sign in the bilateral kidneys (Fig 1). Based on the blood chemistry, urinalysis, and abdominal ultrasonographs, protein losing glomerular disease was diagnosed tentatively. Renal biopsy was performed under sedation with propofol. Histopathologically, glomeruli were markedly diffusely expanded by abundant amorphous eosinophilic material, which was interpreted as amyloid (Fig 2). Therefore renal glomerular amyloidosis was confirmed. Enalapril 0.5 mg/kg (PO, BID) and colchicine 0.03 mg/kg (PO, SID) were administered to decrease proteinuria and serum amyloid protein A release in hepatocytes. The dog also received supportive therapy including daily maintenance fluid, fresh frozen plasma (10 ml/kg), hetastarch (10 ml/kg), sucralfate, antacids, maropitant citrate and force feeding in the hospital. Clinical signs were resolved with these supportive therapies, although abnormal ultrasonographic findings of the bilateral kidneys were persistent. After discharge, the dog received 400 ml of Hartmann solution everyday subcutaneously. Albumin, BUN, and creatinine were monitored every three days to evaluate the necessity for fresh frozen plasma. On the 14th day after the first treatment, this dog no longer needed fresh frozen plasma to maintain the serum albumin level. The serum albumin was maintained with 1.5 to 2.0 g/dl. The serum creatinine level was slightly higher than normal limits but was quite stable for three months. The dog showed good appetite and activity and the client was very satisfactory to the dog's quality of life. After three months, severe azotemia with BUN 123 mg/dl, creatinine 9.3 mg/dl and phosphorus 16.1 mg/dl and nephrotic syndrome with severe hypoalbuminemia (albumin 1.0 mg/dl), proteinuria, peripheral edema and moderate amount of ascites were occurred. The dog was euthanized by the owner's request because there was no response for medical treatments.

Discussion

Amyloidosis is a relatively uncommon genetic or inflam-

[1]Corresponding author.
E-mail : Mcchoi@snu.ac.kr

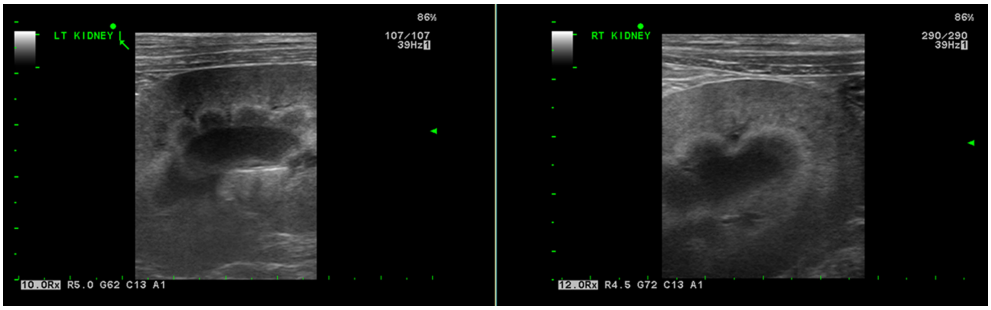

Fig 1. Abdominal ultrasonographs. Hyperechoic renal cortex and hyperechoic medullary rim sign are identified in the bilateral enlarged kidneys.

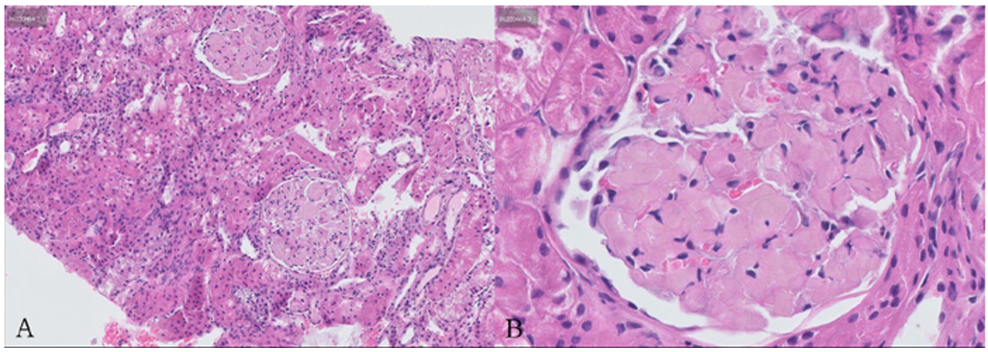

Fig 2. Histopathology. The glomerular loops are replaced by amorphous, finely fibrillar to waxy, and eosinophilic material (B). (A and B, H&E stain. Magnification A = × 200, B = × 400).

matory disease with deposition of beta pleated sheets of amyloid in organ and tissues, damaging normal physiologic function. Amyloid is produced due to aberrant misfolding of cellular protein (1,6,20,21). In dogs, the most common form of amyloid is generated by misfolding of the major acute-phase protein, which is called serum amyloid A. Amyloid A protein depositions are most common in kidneys and directly associated with renal failure in dogs (1,6,9,20,21). It can also be deposited in the liver, spleen, adrenal glands, and gastrointestinal tracts but the clinical signs associated with these organs are not clear. It is quite similar in cats that amyloid deposition can be widespread in the body but the clinical signs are mostly associated with renal amyloidosis, although it is uncommon in cats (3,7,8,17). In the renal amyloidosis, nephrotic syndrome caused by the severe proteinuria and hypoalbuminemia may results in edema, ascites, systemic hypertension or hypercoagulable state in the patient (12,23). The both familial and nonfamilial renal amyloidosis can occur in any age or breed, with increased risk in the older Beagle, Collie, Walker hound, Chinese Shar-Pei, and English foxhound breed in dogs, Abyssinian, Siamese and Oriental short hair breed in cats, although dogs and cats with familial form seem to be usually diagnosed at a younger age (2.3,7-11,16-20).

The renal amyloidosis is one of common glomerular diseases in dogs. Glomerular diseases in dogs and cats include amyloidosis, glomerulosclerosis, glomerulonephritis, IgA nephropathy, hereditary nephritis, lupus nephritis, membranous glomerulopathy, and minimal change glomerulopathy (4.9,13, 19,21). The diagnosis of renal amyloidosis needs renal biopsy. Physical examination, hematology, urinalysis, and ultrasonography help to make presumptive diagnosis of glomerular disease but not the definitive diagnosis of specific glomerular disease. This dog had mild azotemia, hypoalbuminemia, and severe proteinuria with remarkably increased UPC. Ultrasonography is also not specific for renal amyloidosis but enlarged kidneys with increased cortical echogenicity may be associated with glomerular diseases, although these findings cannot distinguish other diffuse renal disease (5). This dog showed remarkable hyperechoic cortex with increased size of bilateral kidneys. This dog also had hyperechoic medullary rim sign, but this sign may represent possibility of renal dysfunction, not specific sign for glomerular disease (15). Other abdominal organs such as liver, spleen, and gastrointestinal tracts were within normal image. Therefore, based on the hematology, urinalysis and ultrasonographs, protein losing glomerular disease was diagnosed tentatively. It is important to differentiate glomerular diseases because definitive diagnosis serves adequate treatment and anticipatable prognosis of the patient. Therefore renal biopsy followed by histopathologic evaluation should be performed. Renal biopsy is relatively safe and indispensable procedure with a low frequency of severe complications. The main complication of renal biopsy is bleeding but not common (13,22). In some familial amyloidosis with medullary involvement, medullary renal biopsy is not recommended because of higher risk of hemorrhage. In concurrent hepatic or splenic amyloidosis, clinically, biopsy of liver or spleen is also not recommended because these organs become more friable and bleed easily than kidney (13,22). However, in the renal amyloidosis with cortical involvement, renal cortical biopsy is helpful for diagnosis relatively safely (13,20,21,22). There were no any com-

plications after renal biopsy in this dog.

Renal amyloidosis is a progressive and fatal disease, so the prognosis is poor. The median survival time was five days (range: 0~443 days) including euthanization (20). Unfortunately, most cases of amyloidosis are diagnosed after the disease has reached an advanced stage. There are no specific treatments to reverse ongoing production of amyloid. The goal of treatment is to maintain patient's quality of life. In order to provide high quality of life of the patient, nephrotic syndrome should be delayed. Nephrotic syndrome is typically characterized by hypoalbuminemia, massive proteinuria and refractory peripheral edema. Renal amyloidosis commonly results in nephrotic syndrome in severely affected dogs (12,23). Aggressive supportive therapies include daily maintanence fluid, fresh frozen plasma, hetastarch, enalapril and cholchicine. Other therapies such as dietary modification, phosphate binder, gastorprotectant, and antiemetic may be needed. Enalapril reduces proteninuria and colchicine is another agent to reduce serum amyloid A protein release from hepatocyte in the liver and to reduce a mediator called amyloid-enhancing factor (13,21). Fresh frozen plasma is expensive but is worthy for critically ill patients with low total plasma protein concentration, active hemorrhage with or without prolongation of coagulation times, persistent vomiting associated with pancreatitis, and sepsis (14). The owner was satisfied with high quality of life in this dog. This dog showed good appetite and activity with aggressive supportive care for three months before azotemia and nephrotic syndrome were deteriorated.

Renal amyloidosis is a life-threatening disease without specific treatment in veterinary medicine so far. However, definitive diagnosis by renal biopsy is needed for predicting an accurate prognosis and focusing on the palliation of a seriously ill patient's symptoms for quality of life.

References

1. Benson MD, Dwulet FE, DiBartola SP. Identification and characterization of amyloid protein AA in spontaneous canine amyloidosis. Lab Invest 1985; 52: 448-452.
2. Bowles MH, Mosier DA. Renal amyloidosis in a family of beagles. J Am Vet Med Assoc 1992; 201: 569-574.
3. Boyce JT, DiBartola SP, Chew DJ, Gasper PW. Familial renal amyloidosis in Abyssinian cats. Vet Pathol 1984; 21: 33-38.
4. Cook AK, Cowgill LD. Clinical and pathological features of protein-losing glomerular disease in the dog: a review of 137 cases (1985-1992). J Am Anim Hosp Assoc 1996; 32: 313-322.
5. D'Anjou MA. Kidneys and ureters. In: Atlas of small animal ultrasonography, Wiley-Blackwell 2008; 342-346.
6. DiBartola SP. The pathogenesis of reactive systemic amyloidosis. J Vet Intern Med 1989; 3: 31-41.
7. DiBartola SP, Benson MD, Dwulet FE, Cornacoff JB. Isolation and characterization of amyloid protein AA in the Abyssinian cat. Lab Invest 1985; 52: 485-489.
8. DiBartola SP, Tarr MJ, Benson MD. Tissue distribution of amyloid deposits in Abyssinian cats with familial amyloidosis. J Comp Pathol 1986; 96: 387-398.
9. DiBartola SP, Tarr MJ, Parker AT, Powers JD, Pultz JA. Clinicopathologic findings in dogs with renal amyloidosis: 59 cases (1976-1986). J Am Vet Med Assoc 1989; 195: 358-364.
10. DiBartola SP, Tarr MJ, Webb DM, Giger U. Familial renal amyloidosis in Chinese Shar Pei dogs. J Am Vet Med Assoc 1990; 197: 483-487.
11. Dubuis JC, Schmid V, Boujon P. Two cases of renal amyloidosis in the Shar pei. Schweiz Arch Tierheilkd 1998; 140: 156-160.
12. Klosterman ES, Moore GE, de Brito Galvao JF, DiBartola SP, Groman RP,
13. Whittemore JC, Vaden SL, Harris TL, Byron JK, Dowling SR, Grant DC, Grauer GF, Pressler BM. Comparison of signalment, clinicopathologic findings, histologic diagnosis, and prognosis in dogs with glomerular disease with or without nephrotic syndrome. J Vet Intern Med 2011; 25: 206-214.
14. Littman, Meryl P. Protein-losing nephropathy in small animals. Veterinary Clinics of North America: Small Animal Practice 41. 2011; 31-62.
15. Logan JC, Callan MB, Drew K, Marryott K, Oakley DA, Jefferies L, Giger U. Clinical indications for use of fresh frozen plasma in dogs: 74 dogs (October through December 1999). J Am Vet Med Assoc 2001; 218: 1449-1455.
16. Mantis P, Lamb CR. Most dogs with medullary rim sign on ultrasonography have no demonstrable renal dysfunction. Vet Radiol Ultrasound 2000; 41: 164-166.
17. Mason NJ, Day MJ. Renal amyloidosis in related English foxhounds. J Small Anim Pract 1996; 37: 255-260.
18. Niewold TA, van der Linde-Sipman JS, Murphy C, Tooten PC, Gruys E. Familial amyloidosis in cats: Siamese and Abyssinian AA proteins differ in primary sequence and pattern of deposition. Amyloid 1999; 6: 205-209.
19. Rivas AL, Tintle L, Meyers-Wallen V, Scarlett JM, van Tassell CP, Quimby FW.Inheritance of renal amyloidosis in Chinese Shar-pei dogs. J Hered 1993; 84: 438-442.
20. Schneider SM, Cianciolo RE, Nabity MB, Clubb FJ Jr, Brown CA, Lees GE. Prevalence of immune-complex glomerulonephritides in dogs biopsied for suspected glomerular disease: 501 cases (2007-2012). J Vet Intern Med 2013; 27 Suppl 1: S67-75.
21. Segev G, Cowgill LD, Jessen S, Berkowitz A, Mohr CF, Aroch I. Renal amyloidosis in dogs: a retrospective study of 91 cases with comparison of the disease between Shar-Pei and non-Shar-Pei dogs. J Vet Intern Med 2012; 26: 59-68.
22. Vaden SL. Glomerular diseases. In: Textbook of Veterinary Internal Medicine, 7th ed. St. Louis: Elsevier Saunders. 2005; 2030-2031.
23. Vaden SL, Levine JF, Lees GE, Groman RP, Grauer GF, Forrester SD. Renal biopsy: a retrospective study of methods and complications in 283 dogs and 65 cats. J Vet Intern Med 2005; 19: 794-801.
24. Watson AD. The nephrotic syndrome due to renal amyloidosis in a dog. Aust Vet J 1971; 47: 398-401.

비글견에서 신장 아밀로이드증 증례

정주현 · 진재봉 · 이현욱 · 최민철[*1]

일산동물의료원, *서울대학교

요 약 : 8년령의 수컷 비글견이 이틀 동안 식욕 부진, 구토, 기력 저하를 주증으로 내원하였다. 혈액학적 검사에서 경등도의 질소혈증과 심각한 저알부민혈증, 뇨 검사에서 심각한 단백뇨가 관찰되었다. 복부 초음파 검사에서 양쪽 신장의 크기가 증가하고 미만성 고에코의 피질이 두드러지게 관찰되었다. 신장 생검과 조직 검사 결과 신장 아밀로이드증으로 확진되었다. 3 개월 동안 환자는 적극적인 내과적 관리를 받았고, 보호자는 환자의 삶의 질에 만족하였다. 이후 심각한 질소혈증과 콩팥증후군이 발생하여 안락사가 실시되었다.

주요어 : 아밀로이드증, 비글, 생검, 신장