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Systemic Amyloidosis in a Cocker Spaniel

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Abstract: A 7-month-old female Cocker spaniel dog was examined for chronic anemia. Based on information provided by local clinician the patient had had a 'flu-like' illness three weeks before submission of the sample, had a fever of 40.9°C, and had mild hepatomegaly. This dog had also history of weight loss, vomiting, anorexia, dehydration, lethargy, ascites, polyuria and polydipsia. A blood smear showed non-regenerative anemia. Thoracic radiograph showed irregular shadowing in the left mid-zone. Serum biochemical results showed a hypercalcemia, azotemia, hypercholesterolemia, hyperphosphatemia, hypoalbuminemia, and metabolic acidosis. Results of urinalysis showed proteinuria, slightly acidic with isosthenuria. Histopathologic examination of tissue sections revealed amyloid deposits in multiple sites including kidneys, liver and spleen.

Key words : Amyloidosis, Nephritic syndrome, Dog.

Introduction

Amyloidosis is characterized by extracellular deposition of a proteinaceous material, amyloid in various tissues and organs. In small animal medicine, these proteins are deposited systemically or locally (2,8). The major forms of systemic amyloidosis recognized in domestic species involve deposition of amyloid that is derived from immunoglobulin light chain, or amyloid that is derived from serum amyloid A, an acute-phase protein synthesized by the liver in response to chronic tissue injury (8).

The most common site of amyloid deposition in doss is kidney (3,5,7,14), but also have been observed in the spleen, heart, liver, adrenal glands, prostate gland, skin, thyroid gland, pancreas, lymph nodes and gastrointestinal tract with more wide tissue distribution in cats (1,10,12,15-17). The consequences of amyloid deposition include chronic renal failure, nephritic syndrome, thrombosis, liver failure, spontaneous liver rupture, arthritis and diabetes mellitus depending on the main organs affected.

Clinical signs vary according to the pattern and extent of tissue dysfunction. Cases often present as sudden death or with acute intermittent signs associated with episodes of intra-abdominal hemorrhage. Involvement of other organs in cats is usually subclinical, although chronic renal failure may develop in affected animals (18). In this report, the authors present clinical and pathological findings of a dog with systemic amyloidosis.

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Case

On 3 October 2005, a seven-month-old female Cocker spaniel weighing 2.9 kg was presented a local clinic with bloody diarrhea of a few days' duration. There was a history of chronic respiratory sign. On examination the dog was thin, with moderate swelling of mandibular lymph nodes. The spleen was enlarged on both palpation and ultrasonography. Decreased number of neutrophils, of which were toxic pattern and decreased RBC mass were seen in the peripheral blood, but other features were normal. Thoracic radiograph revealed enlarged right atrium and ventricular, but no abnormality was detected on lung and liver. On ultrasonography and abdominal radiograph showed no pleural effusion and ascites. Urinalysis indicated a hemolytic state and the Coombs antiglobulin test was positive. Prednisolone therapy (2 mg/kg orally once daily) was tried unsuccessfully until the end of October when the patient presented again with recurring signs of anorectic, polyuria, polydipsia, vomiting and bloody urine.

On 14 November, the patient was referred to the Veterinary Medical Teaching Hospital of Kangwon National University. On arrival, the patient was dehydrated, thin (2.6 kg), fever (39.6°C), bloody feces, and foul-smelling breath. Physical examination and on radiography revealed hepatomegaly, splenomegaly, and irregular shadowing in the left mid-zone. Complete blood count showed a non-regenerative anemia with no Heinz bodies which is usually associated in the case with chemical or onion poisoning (Table 1). Serum biochemical results showed a mild hypercalcemia, azotemia, hypercholesterolemia, hyperphosphatemia, hypoalbuminemia, and metabolic acidosis. Consultation with local clinician who observed spheroyctes in the blood smear, we performed an osmotic fra-

Table 1. Hematological findings in a dog with systemic amyloidosis

CBC		Chemistry	
WBC (10^3/μl)	13.3	Total protein (g/dl)	4.9
RBC (10^6/μl)	4.2	Albumin (g/dl)	2.2
PCV (%)	25.8	ALP (U/L)	589
Hb (g/dl)	7.9	GGT (U/L)	12
MCV (fL)	60.2	Ammonia (μmol/L)	198
MCHC (g/dl)	28.1	Cholesterol (mg/dl)	450
Platelet (10^3/μl)	386	Phosphorous (mg/dl)	8.7
		Calcium (mg/dl)	16.2
		BUN (mg/dl)	58
		Creatinine (mg/dl)	5.2
		CO_2 (mmol/L)	16

gility test, which revealed increased fragility. Urine Dip-stick test result revealed protein 4+, pH 6.5, blood 3+ and specific gravity 1.010. Two days after referral the patient's condition was not relieved, although intensive care was taken. In the meanwhile the patient's owner was refused for further diagnostic testing and medical treatment due to financial burden. On the very next morning, the medical staffs were notified the patient's death.

The dog was autopsied under the owner's written consent. Complete necropsies were performed and tissue samples of all organ systems from each dog were fixed in 10% neutral buffered formalin. Tissues were processed and embedded in paraffin, and 5-8 μm sections were stained with hematoxylin and eosin. In addition, tissue sections of liver, kidney and spleen were stained with Congo red and examined. Abdominal cavity was containing with yellowish serous fluid. The liver was swollen with yellowish spots in the surface (Fig. 1). On microscope, the liver was deposited with eosinophilic amyloid

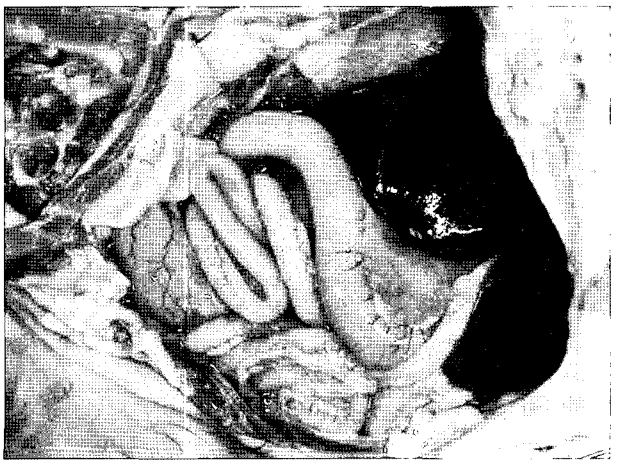

Fig 1. Photomicrograph of abdominal cavity containing with yellowish serous fluid and swollen liver with yellowish spots in the surface and pancreas (left).

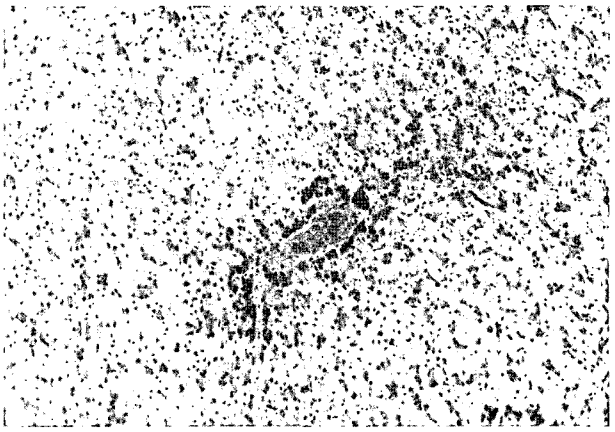

Fig 2. Liver showing homogenous and eosinophilic amyloid deposition between the endothelium and hepatic cords with atrophy of the hepatic parenchyma (HE, ×100, right).

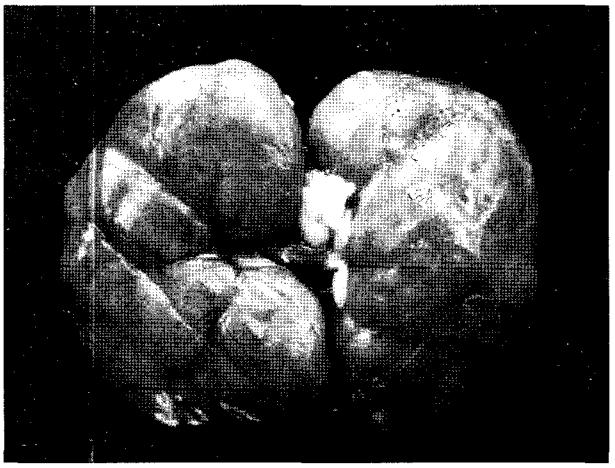

Fig 3. Photomicrograph of kidney showing whitish yellow, firm and irregularly surface was adhered with the thickened capsule (left).

between the endothelium and hepatic cords with atrophy of the hepatic parenchyma (Fig. 2). Kidneys were whitish yellow and irregular pitted surface was adhered with the thickened capsule (Fig. 3). The microscopic renal lesions consisted predominantly of moderate to severe glomerular tufts amyloidosis. Widespread tubular atrophy and mild tubular degeneration were seen throughout the cortices. The interstitum contained scattered groups of lymphocytes and plasma cells (Fig. 4). The hypertrophied glomerular tufts often contained adhesions to the parietal epithelium of Bowman's capsule. Tubules were atrophied, and their basement membranes were thickened. Protein casts were present in the lumens of many tubules. Spleen showing dark red-colored and swelling, and its surface was attached with yellowish white fibrinous strands. Amyloid deposition of the splenic white pulp was also seen (Fig. 5).

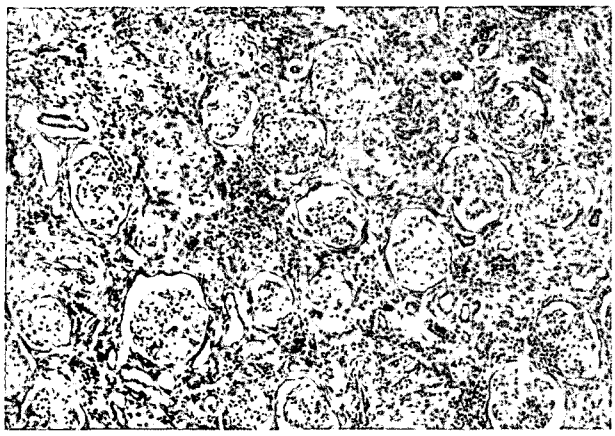

Fig 4. Swollen glomeruli with amyloid deposition in the glomerular tufts. There are prominent proliferation of connective tissue and infiltration of lymphocyte in the interstitum (HE, ×200, right).

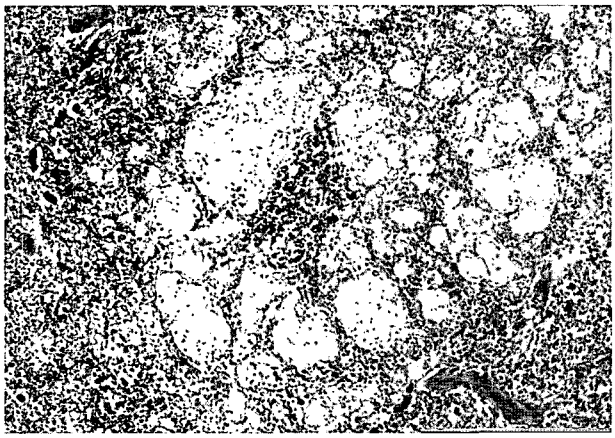

Fig 5. Amyloid deposition of the splenic white pulp. HE, ×200.

Discussion

Amyloidosis can be associated with a number of causative factors and underlying disorders such as chronic inflammation such as blastomycosis, systemic lupus erythematosus, cyclic neutropenia, splenic hemagiosarcoma, infectious, renal dialysis, or neoplastic diseases (7). Familial trait or environmental factors have implicated in some breed of dogs and cats (4,7,8,11).

The most common clinical signs in dogs with amyloidosis are anorexia, polyuria and polydipsia, weakness, lethargy, vomiting, dehydration, and weight loss. The clinical signs observed in the Cocker spaniel of this report were similar and were indicative of chronic renal failure. To the author's knowledge, most of the abnormal biochemistry findings were not satisfactorily resolved in the course of illness while in the local clinic, even supportive care. Although, the prevalence and distribution of complications in renal amyloidosis were not exactly known, we could suspect that thromboembolism and oliguric renal failure may be a complicating factor in this case similar to other studies, in which reported up to 40% of dogs with amyloidosis (6,14). In addition, the dog of this report had amyloid deposits mainly in the kidneys, liver and spleen. The pronounced glomerular involvement observed in the dog agreed with previous findings from two retrospective studies of dogs with renal amyloidosis (6,13), medullary amyloidosis predominated in Chinese Shar pei dogs with familial amyloidosis (7). Bloody urine seen in the patient was suspected the consequence of an intravascular hemolytic event that completed the preexisting amyloid vascular infiltration.

Although serologic testing to assess exposure to potential pathogens such as systemic fungi would have been helpful in identifying predisposing factors, we could not performed because of owner's incompliance related to financial burdens. Ascites, hypoalbuminemia, hypercholesterolemia, azotemia, hyperphosphatemia, severe proteinuria, and isosthenuria with no apparent inflammatory urinary tract disease indicate that the patient developed nephritic syndrome as a complication of renal amyloidosis.

Beagles and Collies have been reported be among the breeds at increased risk for developing amyloidosis and German Shepherd and mixed-breed dogs at low risk (3,6,9). Systemic amyloidosis in cats usually develops those aged under five years, whereas renal one in dogs frequently develops in older groups (6,7,13). Considering 7-month-old of onset in this report potential hereditary predisposition for amyloidosis in Cocker spaniels seems probable, but continued investigation on systemic amyloidosis as a familial problem would be necessary for confirmation. In addition, since breed-related risk factors associated with feline or canine amyloidosis have not been fully defined, further studies are needed to identify possible risk factors responsible for this increased risk and to better define the pathogenesis of amyloidosis in Cocker spaniels.

References

1. Albisser AM, McAdam KPWJ, Perlman K, Carson S, Bahoric A, Williamson JR. Unanticipated amyloidosis in dogs infused with insulin. Diabetes 1983; 32: 1092-1101.
2. Beatty JA, Barrs VR, Martin PA, Nicoll RG, France MP, Foster SF, Lamb WA, Malik R. Spontaneous hepatic rupture in six cats with systemic amyloidosis. J Small Anim Pract 2002; 43: 355-363.
3. Bowles MH, Mosier DA. Renal amyloidosis in a family of Beagles. J Am Vet Med Assoc 1992; 201: 569-574.
4. Chew DJ, DiBartola SP, Boyce JT, Gasper PN. Renal amyloidosis in related Abyssinian cats. J Am Vet Med Assoc 1982; 181: 139-147.
5. 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.
6. 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.
7. 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.
8. Godfrey DR, Day MJ. Generalized amyloidosis in two Siamese cats: spontaneous liver hemorrhage and chronic renal failure. J Small Anim Pract 1998; 39: 442-447.
9. Hargis AM, Stephens LC, Benjamin SA, Brewster RD, Brooks RK. Relationship of hypothyroidism to diabetes mellitus, renal amyloidosis, and thrombosis in purebred Beagles. Am J Vet Res 1981; 42: 1077-1081.
10. Loeven KO. Hepatic amyloidosis in two Chinese Shar pei dogs. J Am Vet Med Assoc 1994; 204: 1212-1216.
11. Piirsalu K, McLean R, Zuber R, Bannister K, Penglis S, Bellen J, Bais R. Role of I-123 serum amyloid protein in detection of familial amyloidosis in Oriental cats. J Small Anim Pract 1994; 35: 581-586.
12. Schwartzman RM. Cutaneous amyloidosis associated with a monoclonal gammopathy in a dog. J Am Vet Med Assoc 1984; 185: 102-104.
13. Slauson DO, Gribble DH, Russell SW. A clinicopathologic study of renal amyloidosis in dogs. J Comp Pathol 1970; 80: 335-343.
14. Slauson DO, Gribble DH. Thrombosis complicating renal amyloidosis in dogs. Vet Patol 1971; 8: 352-363.
15. Tani Y, Uchida K, Uetsuka K, Nakamura S, Nakayama H, Goto N, Doi K. Amyloid deposits in the gastrointestinal tract of aging dogs. Vet Pathol 1997; 34: 415-420.
16. Yano BL, Hayden DW, Johnson KH. Occurrence of secondary systemic amyloid in the pancreatic islets of a cat. Am J Vet Res 1983; 44: 338-339.
17. Yoshino T, Uchida K, Tateyama S, Yamaguchi R, Nakayama H, Goto N. A retrospective study of canine senile plaques and cerebral amyloid angiopathy. Vet Pathol 1996; 33: 230-234.
18. Zuber RM. Amyloidosis in oriental shorthair cats. In: Consultations in feline internal medicine, 3rd ed. Philadelphia: Saunders. 1997: 337-348.

Cocker spaniel 견에서 발생한 전신성 아밀로이드증

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요 약: 7개월된 암컷 Cocker spaniel견이 3주전부터 체중감소, 구토, 탈수, 식욕저하를 보이면서 지속적인 미열을 동반한 다음과 다뇨를 주증상으로 시내 병원에 내원하였다. 담당 수의사의 진료내역을 검토한 결과 복수와 간종대, 혈액도말 검사에서 비재생성빈혈과 흉부방사선 사진에서 좌측 중심부에 불규칙한 음영이 관찰된 것으로 기록되었다. 이후 prednisolone으로 치료하였지만 증상의 경과가 호전되지 않아 정밀진단을 위하여 환자의 혈액을 강원대학교 부속동물병원에 분석, 의뢰하였다. 혈액화학검사에서 고칼슘혈증, 고질소혈증, 콜레스테롤혈증, 고인혈증, 저알부민혈증 및 대사성 산증을 보였으며 뇨검사에서 단백뇨를 동반한 약산성의 등장뇨가 관찰되었다. 임상증상과 실험실 소견에 근거하여 간과 신장에 대한 정밀한 검사를 위하여 입원을 요청하였으나 다음 날 환자는 폐사한 상태로 병원에 후송되었다. 보호자의 동의를 얻어 부검과 조직병리학적인 검사를 실시한 결과 간, 신장, 비장 등의 전신 장기에 과량의 아밀로이드가 침착되어 있음을 확인하였다.

주요어: 아밀로이드증, 신증후군, 개