Severe Secondary Amyloidosis in a Dog with Dermatomyositis

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Summary
A male collie aged 5 years 10 months, which developed dermatomyositis at 2 months of age, died from severe secondary amyloidosis. Amyloid deposition was most severe in renal glomeruli and produced renal failure. Amyloidosis has been reported in man with immune-mediated disorders including rheumatoid arthritis, systemic lupus erythematosus and dermatomyositis. It is possible that the inflammation in this case of familial canine dermatomyositis may have predisposed to the development of amyloidosis.

Introduction
Amyloidosis has developed in persons with immune-mediated disorders including rheumatoid arthritis, dermatomyositis, scleroderma-amyloidosis and systemic lupus erythematosus (Gelderman, Levine and Arndt, 1962; Zilko and Dawkins, 1975; Hollingsworth and Saykaly, 1977; Adu and Cameron, 1982; Orihara, Yanase and Furuya, 1985). Rheumatoid arthritis is the major cause of secondary amyloidosis in man (Hollingsworth and Saykaly, 1977); however, other immune-mediated disorders are less frequently or rarely associated with amyloidosis.

Amyloidosis has also been reported in animals with immune-mediated disorders including: a horse with pemphigus foliaceus and glomerulonephritis (Peter, Morris and Gordon, 1981), beagle dogs with polyarteritis (Harcourt, 1978), a dog with systemic lupus erythematosus (Grindem and Johnson, 1984), rhesus monkeys with rheumatoid arthritis and enterocolitis (Chapman and Crowell, 1977) and a cat with immune-complex nephritis (Saegusa, Shimizu, Nagase and Hasegawa, 1979). In this report, we describe a dog with the immune-mediated disease, familial canine dermatomyositis, which had severe secondary amyloidosis.

Materials and Methods
A male collie (aged 5 years 10 months), a member of a breeding colony of dogs with familial canine dermatomyositis, died of acute renal failure and was necropsied. Samples of most organs were collected in 10 per cent neutral buffered formalin. Tissues were processed, sectioned and stained for histopathological evaluation. Selected sections were stained with Congo red with and without previous potassium
permanganate oxidation, by the method of Wright, Calkins and Humphrey (1977). Minor modification of the staining procedure included covering sections with equal parts of 0.3 per cent H₂SO₄ and 1 per cent KMnO₄ for 10 min.

**Results**

**History**

The collie had been donated to the College of Veterinary Medicine at Washington State University when it was about 4 months old. It had developed mild dermatomyositis at 2 months of age. Skin lesions healed within 10 months, leaving foci of alopecia and hyperpigmentation on the bridge of the nose and hypotrichosis of the tip of the tail. Examination of muscle, obtained by biopsy at 3 years of age, revealed myositis of the superficial portion of the temporalis muscle. Other than cutaneous scarring and occult myositis, the dog had been in good health until 5 days before death. From the 5th day until the morning before death, it was partially anorectic, slightly depressed and vomited yellow fluid and foam a few times each day. The dog ate small quantities of canned food or dog treats, but refused dry dog food. Complete blood count and physical examination three days before death were within normal limits. The vomiting was treated symptomatically with 10 mg metoclopramide every 8 h pending the results of serum analysis. While awaiting the results of this analysis, the dog became severely depressed and vomited a bloody fluid.

It was admitted to the emergency service of the Washington State University Veterinary Teaching Hospital. Blood was drawn for the measurement of blood urea nitrogen (BUN), which was greater than 188 mg per dl. Treatment for renal failure and haemorrhagic gastritis was begun, but the dog died shortly thereafter. Results of initial serum analysis were obtained after the dog had died and showed the following abnormalities: BUN, 140 mg per dl; creatinine, 10.6 mg per dl; inorganic phosphate, 10.8 mg per dl and albumin 2.1 g per dl.

**Necropsy**

Foci of alopecia and hyperpigmentation on the bridge of the nose and hypotrichosis on the tail tip were present. An area of scarring from a previous biopsy was present in the right anterior superficial temporalis muscle. There was slight tan mottling of the left anterior superficial temporalis muscle suggestive of myositis. No gross lesions were seen in other muscles or any joints.

The kidneys were large (left, 99.7 g; right, 106.2 g; body weight, 31 kg). Glomeruli were prominent and there were pale tan streaks in the cortex. The pelvic epithelium was mottled red and tan, was granular and the medulla near the pelvis was pale tan. The urinary bladder was empty.

The pericardial sac contained about 1 ml of blood and a blood clot. The right auricular appendage had a 5 × 10 mm, red to tan area suggestive of myocarditis. Two small red foci (haemorrhages) were present in the epicardium associated with coronary vessels. Similar haemorrhages were seen in the endocardium of the left ventricle and the left atrioventricular valve leaflets.
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The lungs were purplish-red and failed to collapse. Incision released a clear tan fluid from the airways.

The gastric serosa had ecchymotic haemorrhages over one-fourth of the surface. The mucosa was markedly reddened by petechial to coalesced areas of haemorrhage. Blood dripped from the gastric mucosal surface. The small and large intestines were empty. Small haemorrhages were present in association with meningeal vessels.

The gross diagnoses were severe haemorrhagic gastritis, vasculitis of meninges and epicardium, myocardial necrosis and haemorrhage of the right auricle and glomerulopathy. All lesions were compatible with uraemia.

Histopathology

Glomeruli were replaced by eosinophilic homogeneous material which stained orange-red with Congo red stain and had a green birefringence (amyloid) (Figs 1 and 2). The orange-red staining was prevented by previous potassium permanganate oxidation. Amyloid was also present in the interstitium of the renal pelvis and the tunica media of the renal arteries. Lesser quantities of amyloid were also identified as focal or multifocal deposits in the lamina propria of the stomach, small and large intestine, the interstitium of the adrenal gland, thyroid gland, endocrine and exocrine pancreas, mesenteric lymph node, heart and tongue; in the walls of the arteries, veins, or capillaries in the stomach, adrenal gland, spleen, small intestine, pancreas, mesenteric lymph node, liver, tongue, synovium and skin; in the smooth muscle trabeculae and capsule of the spleen; in the wall of a duct in the pancreas; along the basement membrane of the tongue and skin and in the dermis. Other renal lesions included foci of plasma cells in the cortical interstitium and renal pelvic necrosis and haemorrhage.

The gastric submucosa was greatly distended by haemorrhage. Submucosal vessel walls had fibrinoid necrosis. The gastric mucosa was necrotic and haemorrhagic and contained mineral deposits.

Necrosis, haemorrhage and accumulations of neutrophils and lymphocytes were present in the right auricular appendage and focally in the ventricular myocardium. Mineral deposits were present in these areas, as well as in the walls of myocardial vessels. In addition, necrosis of arterial walls and perivascular accumulations of neutrophils and lymphocytes were present.

The lungs were congested. The alveoli contained eosinophilic fluid, neutrophils and macrophages. Mineral deposits were present in the alveolar septa and around the bronchioles.

A few plasma cells were seen in subsynovial areas, but no significant arthritis or synovitis was seen.

A few muscles (cranial tibial, left anterior area of temporalis and diaphragm) had small interstitial lymphocytic foci with or without a few fragmented or vacuolated myofibres.

Moderate hyperkeratosis and acanthosis were present in the skin of the tail. Some arterial walls had eosinophilic homogeneous material, a few erythrocytes and pyknotic cells. The skin of the lips and face had lost its adnexa. A few
Demodex canis were seen in follicles. Other follicles were slightly dilated and thickened by hyperkeratosis and acanthosis. Increased amounts of melanin pigment were present in the dermal macrophages.
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Discussion

Amyloid is deposited in a variety of tissues in response to a variety of disease states. Classification of amyloidosis is somewhat controversial and numerous classification systems have been proposed (Wright and Calkins, 1981). Classifications distinguishing primary (AL protein) and secondary (AA protein) amyloidosis are most frequently used. Primary and secondary amyloidosis are often differentiated by sensitivity or resistance to Congo red staining of the amyloid after pretreatment with potassium permanganate (Wright et al., 1977). In secondary amyloidosis, pretreatment with potassium permanganate eliminates Congo red staining of amyloid deposits. Another feature used to differentiate primary and secondary amyloidosis is the usual absence of chronic inflammatory disease in the primary form. In both forms, the amyloid deposits are usually widespread and affect renal glomeruli (Wright and Calkins, 1981).

Amyloidosis has developed in persons with immune-mediated disorders, most commonly rheumatoid arthritis (Hollingsworth and Saykaly, 1977), but also with dermatomyositis, scleroderma-amyloidosis and systemic lupus erythematosus (Gelderman et al., 1962; Zilko and Dawkins, 1975; Adu and Cameron, 1982; Orihara et al., 1985). Three cases of amyloidosis associated with dermatomyositis in man have been reported in the literature. In one case, the patient also had multiple myeloma and the amyloid deposition may have been associated with multiple myeloma (Zilko and Dawkins, 1975). In another case, the amyloid was secondary and was deposited largely in the skin (Orihara et al., 1985). In the third case, the affected person had no tumour or supplicative processes, the amyloid deposition was generalized, but the type of amyloid deposited was not specified (Gelderman et al., 1962).

Amyloidosis has also been reported in several species of animals with immunological abnormalities (Chapman and Crowell, 1977; Saegusa et al., 1979; Peter et al., 1981), including dogs with systemic lupus erythematosus (Lewis and Hathaway, 1967; Grindem and Johnson, 1984; Jain, 1986). In most of these reports, the type of amyloid deposited was not specified, and organ involvement varied from hepatic to splenic to generalized (Chapman and Crowell, 1977; Harcourt, 1978; Saegusa et al., 1979; Peter et al., 1981).

Familial canine dermatomyositis is a newly recognized disease in collies and Shetland sheepdogs (Shelties) (Hargis, Haupt, Hegreberg, Prieur, Moore, 1984; Hargis, Prieur, Haupt and Collier, 1986a). The condition is a naturally occurring disorder which begins in 2- to 6-month-old dogs and consists of a variably severe dermatitis in the skin over peripheral portions of the body (Hargis et al., 1984; Kunkle, Chrisman, Gross, Fadok and Werner, 1985). Myositis of muscles of mastication and muscles distal to the elbow and stifle develops after dermatitis (Hargis, Prieur, Haupt, Collier, Evermann and Ladiges, 1986b). Vasculitis is present in more severely affected dogs (Hargis, Prieur, Haupt, McDonald and Moore, 1986c). Serum IgG is raised and serum immune complexes are present, sometimes at very high concentrations, and the increase in serum IgG and serum immune complexes corresponds to the severity of the dermatomyositis (Hargis et al., 1986c).

The dog in this report had mild dermatomyositis and secondary amyloidosis with most extensive deposition in renal glomeruli, but no other inflammatory
or neoplastic disease process was identified. At 5 years 10 months of age (age at death), only a few small areas of myositis were present in cranial tibial, temporalis, and diaphragm muscles. It is possible that the inflammation present initially in the skin and followed by inflammation in muscles may have predisposed this dog to development of secondary amyloidosis. In secondary amyloidosis in man, the inflammatory disease predisposing to development of amyloidosis may be mild and in some cases overlooked by physicians (Wright and Calkins, 1981).

As part of previous studies on familial canine dermatomyositis, post-mortem examinations were performed on 20 juvenile to young adult collies, collie-Labrador crossbred dogs, and one Sheltie with dermatomyositis (Hargis et al., 1986a, b), but no evidence of amyloid deposition was found. Shortly after the death of the dog in this report, a complete blood count and measurements of BUN, creatinine, urinalysis and urine protein:creatinine ratio were made on the remaining four dermatomyositis-affected collies in the breeding colony. No abnormality was detected. To the authors’ knowledge, the dog in this report is the first dog with dermatomyositis to develop severe secondary amyloidosis.

References


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