Systemic amyloidosis in cats

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Aetiology & Pathogenesis

Amyloidosis is potentially the result of a variety of disease processes which lead to the deposition of extracellular (intercellular) fibrillar protein material (amyloid). There are several different types of amyloid, but they have a similar appearance due to the physical conformation of the fibrils (a b-pleated sheet).

The pathogenesis of amyloidosis involves the excessive production of the amyloidogenic protein, and/or defective proteolysis, and/or a structural abnormality of the protein. In some species, some normal proteins are amyloidogenic (if present in sufficient concentrations will be deposited in tissues as amyloid) and disease may develop in association with excessive production of such proteins and/or reduced removal/proteolysis. Other cases of amyloidosis are associated with the production of abnormal proteins by cells or normal proteins that have an abnormal structure (eg, due to genetic defects) that renders them amyloidogenic. The b-pleated sheet configuration of amyloid is responsible for the insolubility of the fibrils, and its resistance to proteolysis. Although inert, the deposition of amyloid within organs can result in progressive interference with normal function and blood flow, and may result in necrosis and fibrosis.

Three types of systemic amyloidosis are recognised in humans:
• Immunoglobulin-related
• Reactive
• Heredo-familial

Immunoglobulin-related amyloidosis:

Immunoglobulin-related amyloidosis is where the amyloid protein is a degradation product of the light-chain from an immunoglobulin (eg, has been reported in association with multiple myeloma and paraproteinaemia). Immunoglobulin-related amyloidosis has been described in a variety of different species, including the cat (in association with IgG-related myeloma), but is rare.

Reactive amyloidosis:

In reactive amyloidosis, the amyloid precursor is an acute phase protein (an alpha-1 globulin) which can be elevated in a number of infectious, inflammatory, and neoplastic disorders. The protein is known as serum amyloid-A related protein (SAA), and is formed in the liver by hepatocytes. In reactive feline amyloidosis, amyloid deposits have been found in the endocrine and exocrine pancreas, liver, spleen, adrenals, thyroids, parathyroids, small intestine, stomach, lung, heart, tongue, and kidneys. Despite the generalised nature of the deposits, the heaviest deposits occur in the liver and kidneys. In a few cases, the kidney may be the only organ involved.

In most cases of feline reactive systemic amyloidosis, the underlying cause is unknown. Amyloid deposits are primarily found in the medullary interstitial space of the kidney in the cat, cortical and glomerular involvement may also occur but to a lesser extent. This contrasts to the situation in the dog where the amyloid is deposited primarily in the glomerulus and results in proteinuria. Clinical signs in the cat are related to reduced renal function and subsequent uraemia. Amyloidosis is seen in a wide age range of cats (1-17 years), but usually affects older cats (mean 7.5 years). There is no sex predisposition.

Familial amyloidosis in Abyssinian/Somalis and in Siamese/Orientals:

In man, SAA or other proteins (eg. pre-albumin) can be involved in familial disease.

An hereditary, familial amyloidosis is recognised in Abyssinians, the amyloid is again formed from SAA, and clinical signs are again usually related to renal disease. The average age of onset of signs is 3-3.5 years, and the disease may be more common in females. There is great variation between individuals in the progression of the disease; in some, amyloid deposition is rapid and severe with rapid progress of clinical signs, whilst in others deposition is slow with only gradual progression of signs. Only 75% of cats have glomerular involvement, and medullary involvement is predominant. SAA protein has been shown to be very highly elevated in Abyssinians with familial amyloidosis, and also appears to be somewhat elevated in normal Abyssinian cats, however because of a very wide range in values, Abyssinians with familial amyloidosis could not be distinguished from healthy Abyssinians, or from other cats with inflammatory or infectious conditions on the basis of SAA concentrations. High SAA concentrations are clearly necessary for amyloidosis, but are also clearly not the only factor.

A substantial number of publications have now appeared of systemic amyloidosis in Siamese and Oriental cats. In contrast to Abyssinians where the kidneys are usually the most severely affected site, in many of these cats the liver is more severely affected. Controversy has existed as to the aetiology of these cases and whether it represents an hereditary or an inflammatory (reactive) disease. Current research suggests that it is probably a combination of both factors with mutations resulting in amino acid substitutions that renders the serum
AA protein more amyloidogenic, but probably coupled with (at least in many cats) inflammatory disease processes that affect production of SAA and thus alter the phenotypic expression of disease. Further studies are necessary to clarify the heritability of the disease in these breeds.

Clinical signs
Although signs of chronic renal failure predominate in many cats, if there is an infectious or inflammatory disease underlying the amyloidosis, clinical signs attributable to this primary disease may predominate. Similarly laboratory data show the effects of renal disease, occasionally with evidence of the primary disease. In other cats, the amyloidosis will predominantly affect the liver with spontaneous intra-abdominal haemorrhage being the most common presentation - many cats may have recurrent non-fatal episodes (anaemia that spontaneously resolves) before suffering a severe fatal haemorrhagic episode. In some cats, both hepatic and renal signs occur together.

Diagnosis
Diagnosis can only be made by renal biopsy (or biopsy of other affected tissue). Once diagnosed, attempts should be made to identify and treat any underlying disorder, however a primary disease is rarely found in cats. The prognosis for cats with amyloidosis remains grave.