

Reportes de caso

Glomerular variant of systemic amyloidosis in an Abyssinian cat Variante glomerular de amiloidosis sistémica en un gato Abisinio

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Resumen

La amiloidosis es una enfermedad caracterizada por la deposición de un material proteináceo amorfo, hialino, y eosinofílico. Un gato macho abisinio de 4 años manifestó enfermedad; los tejidos fijados en formol fueron procesados por la técnica de hematoxilina-eosina y sometidos a examen histopatológico. La historia clínica registró signos gastrointestinales, cambios de comportamiento y mala condición corporal. En la evaluación histopatológica se encontró material extracelular eosinofílico amorfo en glomérulos renales, espacio de Dissé en hígado y alrededor de las glándulas de los intestinos grueso y delgado. Los tejidos teñidos con rojo Congo revelaron un material con birrefringencia verde al microscopio con luz polarizada. Adicionalmente, se observaron úlceras en colon, peritonitis y vasculitis que podrían estar relacionadas con la patogénesis de la amiloidosis en este caso.

Palabras clave: Felino, amiloide, rojo Congo

Abstract

Amyloidosis is a disease in which a proteinaceous amorphous, eosinophilic, hyaline material is deposited extracellularly. A 4 year old Abyssinian male cat manifested disease; formalin fixed tissues were processed by the hematoxylin – eosin technique and submitted to histopathological examination. The clinical history included gastrointestinal signs, behavioral changes and poor body condition. In the histopathological evaluation an eosinophilic irregular-shaped extracellular material located in renal glomeruli, in the Dissé space of liver and around the glands in the large and small intestines. Affected tissues stained with Congo red revealed a material with green birefringence when examined under polarized light. Colonic ulcers, peritonitis and vasculitis were also seen and could be related to the pathogenesis of the amyloidosis in this case.

Keywords: Feline, amyloid, Congo red

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Amyloidosis is a group of diseases in which amyloid, an eosinophilic, irregularly-shaped, homogeneous, hyaline proteinaceous material, is deposited extracellularly in the walls of small vessels of several sites in different organs with the liver, spleen and kidneys being the most commonly affected. In the kidneys, the amyloid usually accumulates in the glomeruli in most domestic animals; however, it has also been noted to accumulate in the medulla of the kidney in Sharp-pei dogs and cats (Maxie & Newman, 2007). The diagnosis of amyloidosis requires histopathologic identification by hematoxylin-eosin of amyloid

deposits in affected tissues. This is confirmed by Congo red stain, the highly ordered structure of the amyloid fibrils confers to the deposits stained with Congo red, a typical apple-green birefringence under polarized light (Obici, *et al.*, 2005; Chew *et al.*, 2011a; Woldemeskel, 2012). The use of Thioflavin-T special stain, immunohistochemistry and electron microscopy have been also reported in animals (Boyce *et al.*, 1984; Van der Linde-Sipman *et al.*, 1997).

The pathogenesis of amyloidosis is believed to be due to an excessive production of amyloidogenic proteins, and/or defective proteolysis and/or structural abnormality of the proteins. An alpha-pleated configuration of amyloid protein is responsible for the insolubility of the fibrils and its resistance to proteolysis (Sparkes, 2007; Woldemeskel, 2012).

In domestic animals, most cases of amyloidosis are of the reactive type and both systemic and localized forms can occur. Systemic amyloidosis in cats of the Abyssinian breed is well described and occurs as a familial trait involving several organs such as the liver, spleen and kidney. (Maxie & Newman, 2007; Khoshnegah & Movassaghi, 2010).

In this report, we describe a systemic case of reactive amyloidosis in an Abyssinian cat, in which amyloid was deposited mainly in most glomeruli of the kidney instead of the medulla and renal papilla as described in previous reports for this breed. The presence of amyloid in this case was confirmed by a Congo red stain.

Case report

A 4-year-old male Abyssinian cat from Bogotá, Colombia, was presented to the referring veterinarian with a history of persistent diarrhea, vomiting, anorexia and marked temperamental changes (E.g. aggression, unrest, irritation). Clinically, the body condition of the individual was 1/5, the mucous membranes were pale and mucosal capillary refill time was 2 seconds. The ultrasonographic examination revealed liquid in the abdominal cavity. The patient showed progressive wear and he eventually died. The necropsy was performed and samples of kidney, liver, small and large bowel, lung, adrenal glands, mesenteric lymph nodes and spleen were fixed in 10 % formalin and submitted for microscopic examination to the diagnostic laboratory of the National University of Colombia, Bogotá.

Histologically, in the kidneys, all glomeruli were enlarged and obliterated the Bowman's space. Eosinophilic, amorphous and acellular material compatible with amyloid accumulated in the mesangial matrix (Fig 1). Some glomeruli adhered to the Bowman's capsule (Renal glomerular synechia). Similar eosinophilic material also accumulated in the basement membrane of some tubules and in the tunica intima of several renal blood vessels. Multiple hyaline drops in the tubular epithelium, moderate formation of hyaline casts and sloughed epithelium and generalized dilation of the renal tubules were also found (Fig

2). Occasional foci of lymphocytes and plasma cells infiltrated the interstitium. In the liver, there were similar accumulations of eosinophilic, acellular and irregularly-shaped material under the sinusoidal endothelial cells causing dilation of the space of Disse. This finding was accompanied by sinusoidal dilation and atrophy of hepatocytes. Affected hepatocytes contained biliary pigments and vacuoles in the cytoplasm. In the large intestine, there were large ulcers covered by fibrin and the adjacent mucosa had microthrombus, hemorrhages, eosinophilic amorphous material surrounding the glands, and lymphoplasmacytic, histiocytic and neutrophilic inflammation (Fig. 3). In the submucosa and muscular layers, there was edema and moderate dilation of lymphatics. The villi of the small intestine were atrophic, the Lieberkühn glands were dilated and similar eosinophilic, acellular and irregularly-shaped material as in the kidneys, liver and large intestine was observed around the glands and blood vessel walls of this organ. In the peritoneum, there were foci of lymphocytes and plasma cells, microthrombi and vasculitis. In the spleen and lymph node, a severe mixed lymphoid depletion was evident, with neutrophils infiltration and evidence of haematopoiesis, the remaining organs did not show important changes.

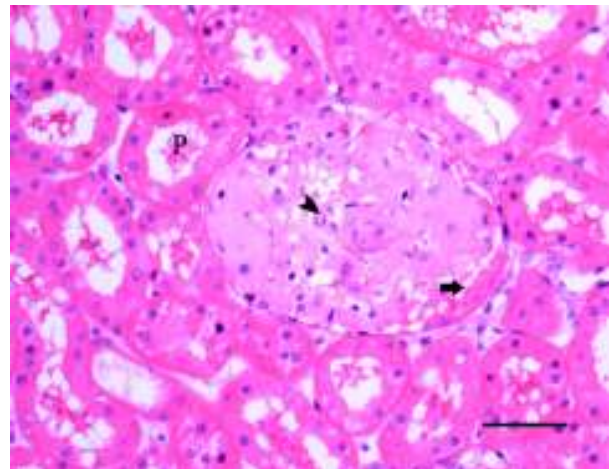


Figure 1. An affected glomerulus. The eosinophilic and amorphous material occupies and distorts most of the glomerulus structure leaving only one recognizable capillary (Arrowhead). Proteinuria is visible in the remaining space of Bowman (Arrow) and in the lumen of tubuli (P). Hematoxylin and eosin. Bar=50 μ m

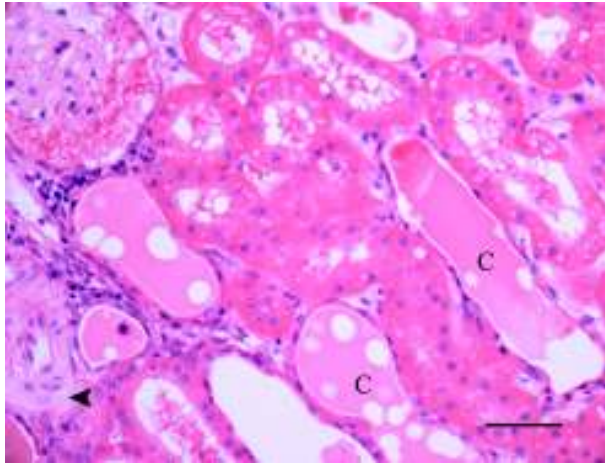


Figure 2. Kidney, another aspect for the lesions. On the top left an affected glomerulus with proteinuria in the space of Bowman. A lympho-plasmocytic infiltrate surrounds the glomerulus and other structures. The wall of the arteriole on the extreme left seems to be affected by a fibrillar amorphous eosinophilic material. Proteinuria and hyaline casts (C) in the lumen of tubules are seen. Hematoxylin and eosin. Bar=50 μ m.

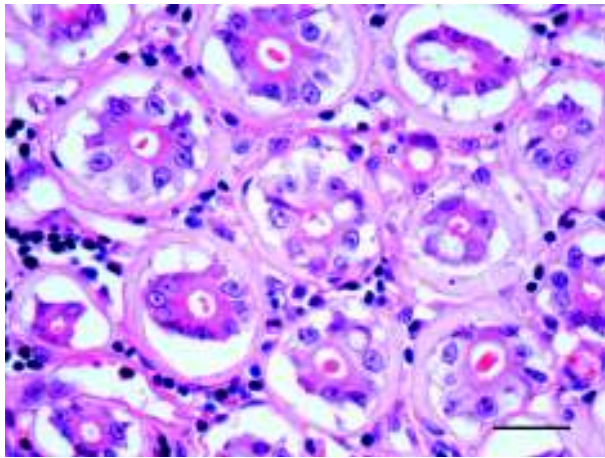


Figure 3. Large intestine. The eosinophilic amorphous material surrounds all glands, probably, it is deposited within the basal membrane. Hematoxylin and eosin. Bar=50 μ m.

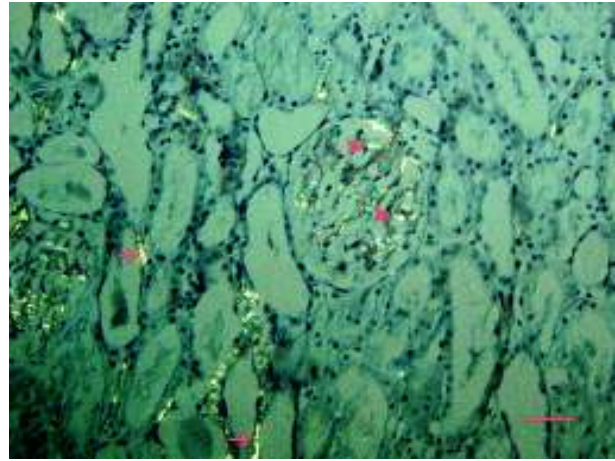


Figure 4. Kidney. Green apple birefringence is observable in what appears to be mesangial matrix of a glomerulus (Arrowheads). Also, multiple foci of birefringence under the tubular epithelium are visible (Arrows). Polarized light microscope. Congo red staining. Bar=50 μ m

Under the polarized light microscope and with the Congo red stain, green birefringent material was observed in the kidney -mainly within the glomeruli but also under the tubular epithelium- (Fig. 4).

Based on the breed, history, and histopathologic features, a final diagnosis of systemic amyloidosis was made, consistent with the well-known familiar hereditary trait in the Abyssinian breed; however, an infection with the feline infectious peritonitis virus and/or a secondary systemic bacterial infection that probably originated from the colonic ulcers cannot be ruled out and could have complicated this case.

Discussion

Amyloidosis is an uncommon disease in domestic animals that has been observed in dogs and cats. In cats, this condition is observed in Abyssinian, Siamese and Oriental breeds of cats (Boyce *et al.* 1984; Maxie & Newman, 2007). In this report, a case of systemic amyloidosis in an Abyssinian cat was described, which showed most of the findings reported previously for this entity in this breed. The Congo red stain under polarized microscope confirmed the identity of the eosinophilic, acellular and irregularly-shaped material accumulating in different organs as amyloid, which was demonstrated by an apple green birefringence.

Histologically, the amyloid was deposited in the typical organs reported in this breed such as the

liver, spleen, intestine and kidneys; however, there was no amyloid deposition in the renal medulla and papilla as described as frequent by Chew *et al.* (1982) and Boyce *et al.* (1984). Instead, most of the amyloid was deposited in renal glomeruli (Probably in the mesangial matrix) with some deposits under the tubular epithelium, visible only with the Congo red technique. In this case, we found that the Congo red stain was reliable to detect the amyloid, contrary to the difficulty reported in cats by Boyce *et al.* (1984). Additional staining with thioflavin T was not required to make the diagnosis.

Epidemiologically, amyloidosis is a rare disease in felines with incidences of 1 per 300 up to 7 per 100 cats (Clark & Seawright, 1969), and a prevalence of 5% in Abyssinian cats (Van der Linde-Sipman *et al.*, 1997). The most frequent age of presentation in this breed is between 1 to 5 years without a gender predilection (Chew *et al.*, 1982).

Amyloidosis in Abyssinian cats was first documented in 1982. Controversy still exists regarding the etiology of these cases and whether it represents a hereditary or inflammatory disease (Chew *et al.*, 1982). Recent reports suggest that several factors are probably responsible for the development of this condition such as mutations resulting in substitutions that make the serum AA protein more amyloidogenic, although in many cats it is also associated with inflammatory diseases that affect SAA production and altering the phenotype of the disease (Jiménez *et al.*, 2011). In any case, it is important to keep in mind that in the majority of affected dogs and cats, the predisposing cause for amyloidosis cannot be determined (DiBartola & Benson, 1989). Our results suggest that multiple infectious diseases such as a putative feline infectious peritonitis (FIP) virus and/or a probable bacterial infection originating from the colonic ulcers could be related to the pathogenesis of the amyloidosis in this case and may have also contributed to the poor condition of this cat. Some studies have reported an association between FIP and systemic reactive amyloidosis, including cases of Abyssinian cats, where a particular importance is given to the serum amyloid A protein (SAA), this protein can show up to a 10-fold increase in cases of FIP (Van der Linde-Sipman *et al.*, 1997; Godfrey & Day, 1998; Giordano *et al.*, 2004).

In this case, there were not clinical manifestations of renal insufficiency or renal tissue lesions characteristic of renal failure, but glomerular and

tubular changes, and the formation of hyaline casts are indicative of a protein-losing nephropathy. Amyloid deposition is not restricted to the kidneys in Abyssinians with amyloidosis, and deposits are frequently found in other organs (E.g., adrenal glands, thyroid glands, spleen, stomach, small intestine, heart, liver, pancreas, colon) as those found in this case; nonetheless, amyloid deposits in these other organs do not appear to make an important contribution to the clinical syndrome (Chew *et al.*, 2011b).

The inheritance type of amyloidosis in Abyssinian cats seems to be a dominant autosomal trait with variable penetrance. The amino acids of the AA amyloid protein in Abyssinian cats differs slightly from that of Oriental and Siamese cats, perhaps explaining the predilection for amyloid deposition in the liver in these two breeds (Van der Linde-Sipman *et al.*, 1997; Niewold *et al.*, 1999; Chew *et al.*, 2011).

In conclusion, we report and provide photographic evidence of a glomerular variant of systemic amyloidosis in an Abyssinian cat in which amyloid is deposited in renal glomeruli rather than the renal medulla and papilla as usually reported for this breed. The most likely cause of this cat's poor condition was simultaneous infection with feline infectious peritonitis virus and bacterial septicemia secondary to ulcers in colon. The amyloid material in the affected organs was confirmed microscopically by using a Congo red stain, which gave a green birefringence under polarized light.

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