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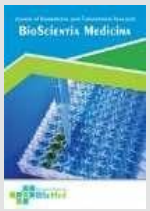

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Renal Amyloidosis: A Narrative Literature Review

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A B S T R A C T

Amyloidosis is a disorder in which soluble proteins aggregate and are deposited extracellularly in tissues as insoluble fibrils, causing progressive organ dysfunction. Amyloid fibril formation begins with misfolding of amyloidogenic precursor proteins. The fibrils have a characteristic appearance by electron microscopy and produce double refraction under polarized light when stained with Congo red dye. Classification of amyloidosis is based on the precursor proteins that form amyloid fibrils and the distribution of amyloid deposition both systemically and locally. The main form of systemic amyloidosis; AL amyloid, AA amyloidosis, ATTR amyloid. The kidney is the organ most frequently involved in systemic amyloidosis. Systemic amyloidosis may originate from anomalous proteins, such as immunoglobulin light chains or serum amyloid protein in chronic inflammation or may arise from hereditary disorders. The clinical manifestations of renal amyloidosis vary with the type of amyloid protein and the location and extent of amyloid deposition. Treatment of amyloidosis should be a two-part process; managing symptoms and reducing or stabilizing amyloid protein. Treatment of amyloidosis is focused on reducing the production of amyloidogenic proteins and inhibiting their aggregation.

1. Introduction

Amyloidosis is a disorder caused by extracellular tissue deposition of insoluble fibrils that can cause a wide spectrum of symptoms depending on the type, location, and amount of deposition. Amyloidosis can be divided into systemic or local diseases. The four most common types of amyloid are immunoglobulin light chain (AL), amyloid A (AA), transthyretin (ATTR), and amyloid Beta peptide (AB).[1] Systemic amyloidosis is categorized into primary and secondary amyloidosis, which carries the risk of progression to neoplastic disease. Systemic amyloidosis generally affects tissues such as the kidneys, heart, peripheral nerves, and musculoskeletal tissue. On the other hand, local Amyloidosis is rare and has a different character compared to systemic amyloidosis. In fact, localized Amyloidosis has never been known to develop systemically. Local amyloidosis is generally found in the upper respiratory tract (nasopharynx, tongue), orbit, and urinary tract, including the bladder and musculoskeletal tissue (skin and nails).[2]

Without treatment, amyloidosis can ultimately be fatal due to progressive multisystem organ failure. The kidney is one of the most common organs involved with AL amyloidosis, with several series describing clinically evident renal disease in 48% – 82% of patients. New technologies, such as mass spectrometry, have enabled early diagnosis and can recognize fibrils of new pathogens. Furthermore, these advances allow for improved stratification and treatment options. Treatment for amyloidosis varies based on the pathogenic fibrils, the severity of the disease, and organ involvement.[3]

Epidemiology

The prevalence of systemic amyloidosis increases every year. In a review of 11,006 patients referred to the UK National Amyloidosis Center (NAC) between 1987 and 2019, referrals increased sixfold, with systemic AL amyloidosis being the most common diagnosis, accounting for 55% of the total.[4] In research, women experience AL amyloidosis less frequently. AL amyloidosis is more common in men.[5]

Type

The type of amyloid is determined by the precursor protein amyloid fibrils and determines the clinical phenotype, management, and prognosis.[4] Determination of different types of amyloidosis is indistinguishable by light or electron microscopy. The most direct method for identifying amyloidogenic proteins is by mass spectrometry or amino acid sequencing of proteins extracted from amyloid deposits. This technique is not routinely available and is usually not necessary unless other approaches cannot identify it. The most definitive method used in the clinical setting is immunofluorescence or immunohistochemical staining of tissue using antibodies directed against known amyloidogenic proteins. However, less direct methods are often required due to a lack of sensitivity or availability of antibody reagents.[3]

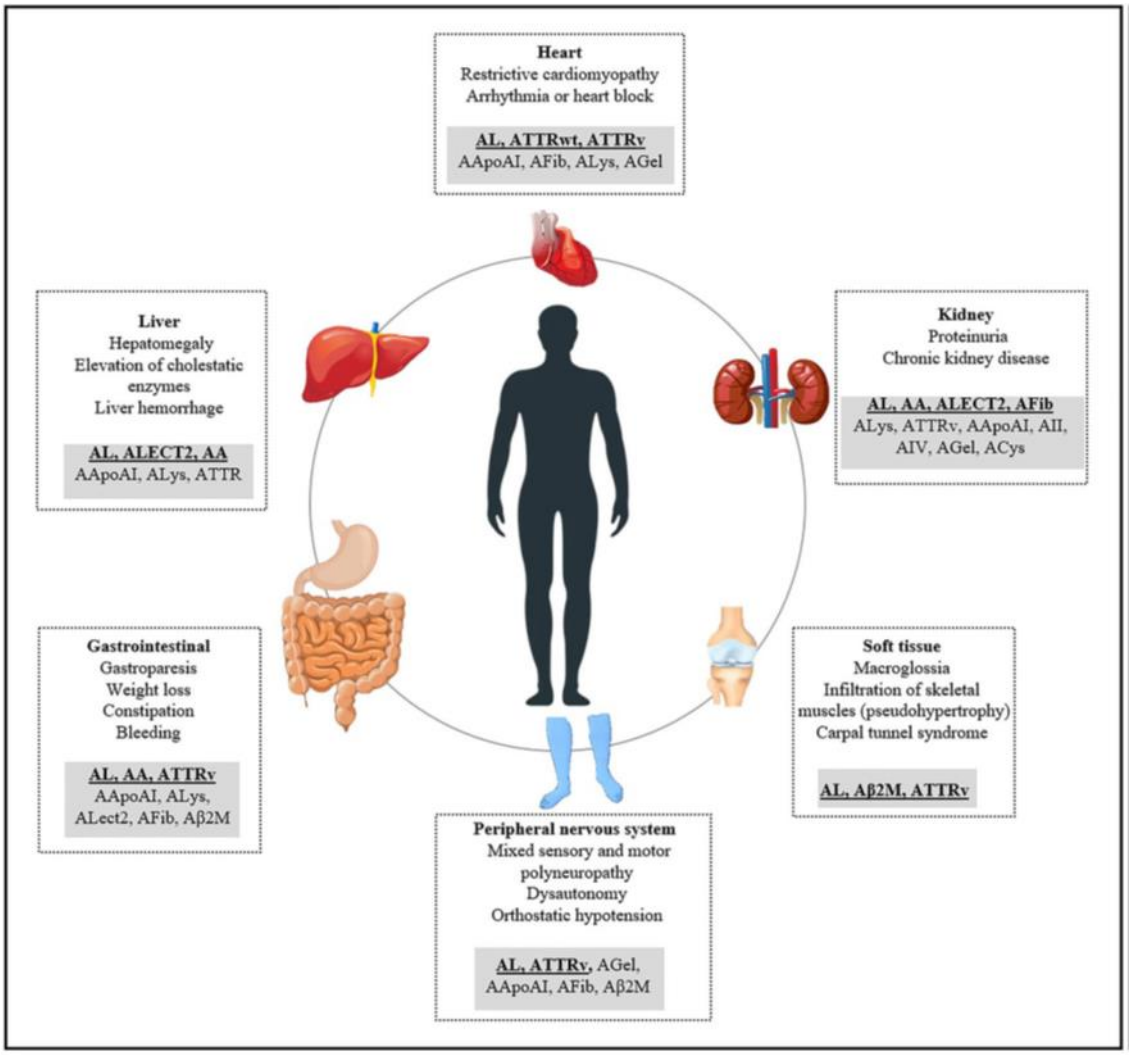

Figure 1. Division of amyloidosis based on location.[6]

Explanation of types of amyloidosis as in Figure 2. Two main types of amyloidosis in the kidney are immunoglobulin light *chain* (AL) Amyloidosis, which is associated with plasma cell dyscrasias, and Amyloidosis amyloid A (AA) secondary to chronic inflammatory conditions.[3,7]

AL Amyloidosis accounts for the largest number of cases, followed by AA Amyloidosis in most studies published in Western Countries.[7]

Table 1. Types of amyloidosis.

			Organ involvement					
	Fibril precursor protein	**Underlying pathology**	**Cardiac**	**Kidneys**	**Liver**	**Nerves**	**Additional clinical findings**	**Treatment**
AL	Monoclonal light chain	Plasma cell dyscrasia	70%	50%	16%	23%	Macroglossia, periorbital bruising, nail dystrophy	Chemotherapy and/ or ASCT
wtATTR	Wild-type transthyretin	None	100%	0%	0%	0%	Carpal tunnel syndrome, spinal stenosis, aortic stenosis	TTR stabilizer or gene silencing therapy
hATTR	Variant transthyretin	Abnormal TTR gene	∞[a]	Rare		∞[a]		
AA	Serum Amyloid A	Chronic Inflammation or infection	1%	97%	23%	0%	Features of underlying inflammatory disorder	Control of inflammation
ALECT2	LECT2	Unknown	0%	92%	46%	0%	None	Supportive
AFib	Variant fibrinogen	Abnormal fibrinogen gene	0%	100%	3%	1%	Cardiovascular disease	Supportive
AApoA1	Variant ApoA1	Abnormal ApoA1 gene	-[a]	-[a]	-[a]	-[a]	Renal, liver, and cardiac involvement are common	Supportive

[a] : Organ involvement depends on specific gene mutations.

AL amyloidosis (immunoglobulin light chain amyloidosis) or amyloidosis primer

Systemic AL amyloidosis occurs as a result of the production of abnormal amyloidogenic monoclonal light chains from the clonal basis of dyscrasia. The median age of diagnosis was 63 years, with 1.3% diagnosed at less than 34 years of age. Involvement Multi-organ occurs frequently, with renal involvement in 58%, cardiac involvement in 71%, and cardiorenal involvement in 38%. The gastrointestinal, hepatic, soft tissue and peripheral and autonomic nervous systems may also be affected. Clinical presentation depends on organ involvement, with proteinuria, renal impairment, and rapidly progressive symptoms most commonly non-specific, such as weight loss, weakness, and fatigue. Patients can come from almost any medical specialty, and a high index of suspicion is key to early diagnosis before significant organ damage occurs.[4] It is certain that cardiac involvement is the main prognostic determinant in AL Amyloidosis. and if diagnosed late and not treated, most patients can lead to death.[8]

The diagnosis is often established based on renal biopsy or following the development of proteinuria (40.5 g/24 hours) in patients with a previous diagnosis of AL. Investigation of AL requires the identification of monoclonal Ig. Detection is most often achieved using serum and urine protein electrophoresis, serum and urine protein immunofixation, and/or serum free light chain (sFLC) dosing, techniques that are sensitive to the identification of the monoclonal Ig component in 65, 73, and 88% of each case.[6]

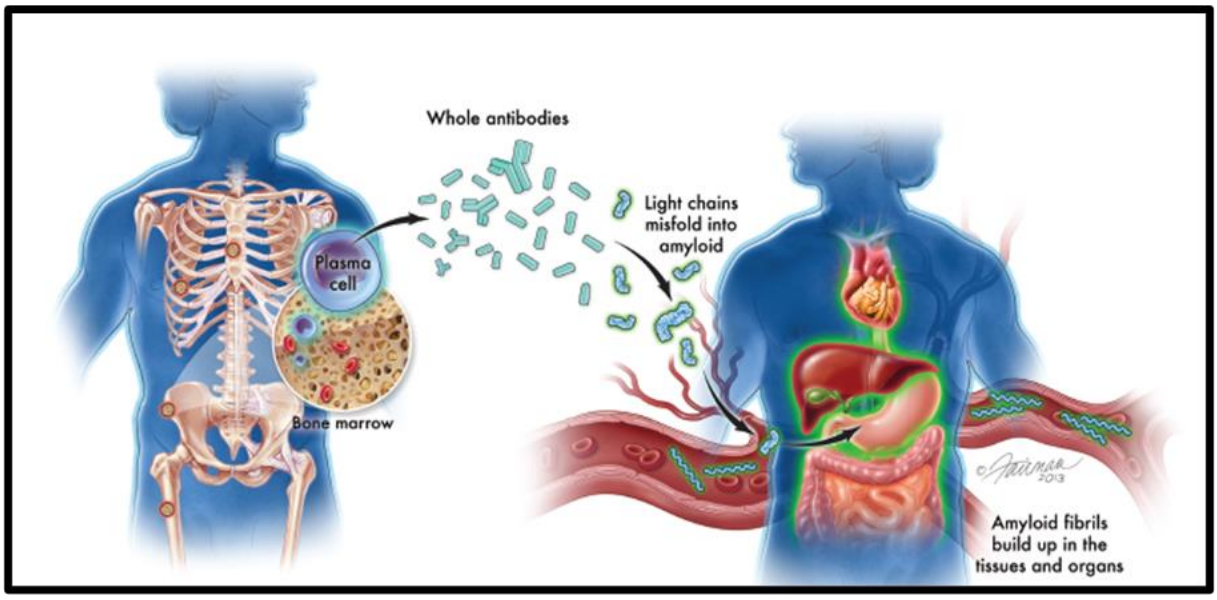

Figure 2. Accumulation of abnormal amyloidogenic monoclonal light chains in the blood and deposited in various tissues.[9]

AA amyloidosis or secondary amyloidosis

Systemic AA amyloidosis is usually seen with renal dysfunction and occurs as a complication of prolonged elevations in serum amyloid A (SAA) protein concentrations. Concentrations of SAA, an acute phase reactant, are increased in chronic inflammatory conditions such as chronic arthritis (60%), chronic sepsis (15%), periodic fever syndrome (9%), and inflammatory bowel disease (5%). Infiltration of the kidneys and spleen by amyloid is common at diagnosis, and cardiac amyloidosis is rare (<1%). The increasing use of biological therapies, allowing better control of some inflammatory conditions, has been associated with a decrease in the incidence of systemic AA amyloidosis. Renal biopsy demonstrated moderate to severe glomerular involvement in all cases, most commonly including nodular mesangial amyloid deposits. Vascular involvement is seen in 95% of biopsies, in addition to interstitial and tubular basement membrane involvement. IHC-based staining for amyloid A can be used for diagnostic confirmation.[6,9]

Familial amyloidosis (ATTR) or hereditary amyloidosis

ATTR amyloidosis is caused by amyloidogenic transthyretin (TTR) protein and is subdivided based on the TTR genotype into acquired wtATTR amyloidosis and hereditary variant ATTR amyloidosis (vATTR) Amyloidosis, the latter of which is associated with pathogenic mutations in the TTR gene, mutations of which are now more than 130. TTR is a protein that helps transport thyroxine (thyroid hormone) and retinol (vitamin A) in the body.[9] WtATTR amyloidosis typically presents as a restrictive cardiomyopathy (i.e., ATTR-CM) with a history of soft tissue disease such as carpal tunnel syndrome, spinal stenosis, biceps tendon rupture, or osteoarthritis, often predating the diagnosis by years. The median age at diagnosis of wtATTR-CM was 79 years, and there was a male predominance (94% in the UK cohort). vATTR amyloidosis is more heterogeneous, although it is most often dominated by heart failure, neuropathy, or a combination of both. There is an association between the clinical phenotype and the specific cause of the TTR mutation. Rarer causes of renal amyloidosis include leukocyte chemotactic factor 2 (ALECT2) amyloidosis, hereditary Aa chain fibrinogen

amyloidosis (AFib), hereditary lysozyme amyloidosis, hereditary apolipoprotein A-I (AApoAI) and apolipoprotein A-II (AApoAII) amyloidosis, and hereditary apolipoprotein C- II (AApoCII) and apolipoprotein C-III (AApo- CIII) Amyloidosis, which with the exception of AApoAI and AApoCIII Amyloidosis, rarely involves the heart.[4]

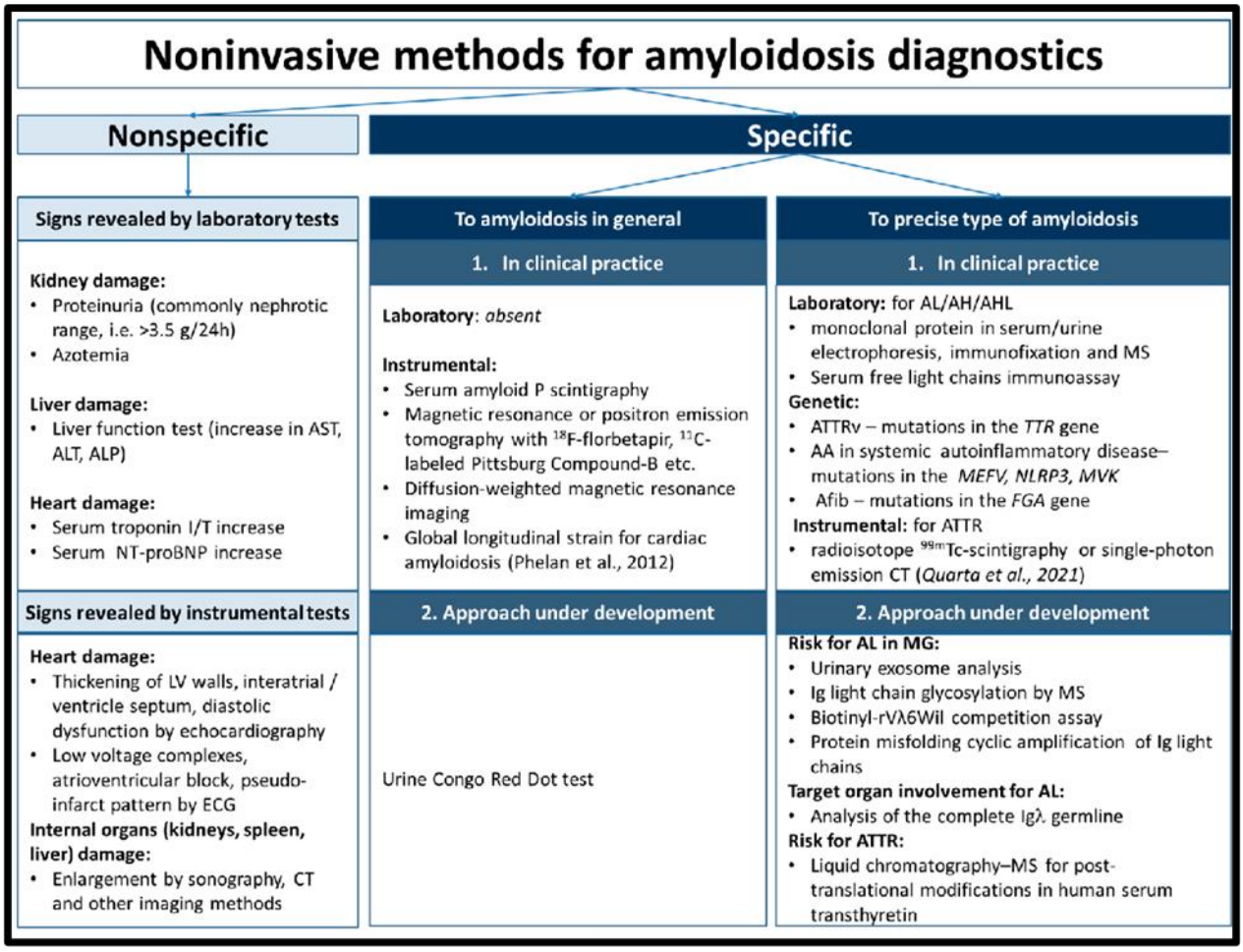

Figure 3. Chart of non-invasive methods for diagnosis.[10]

Pathogenesis

The initial steps for fibrillogenesis and amyloid formation include protein misfolding, which can occur as a result of proteolytic cleavage. Protein misfolding has a tendency to self-aggregation and subsequent generation of fibrils.[11] During amyloid formation, intermediate proteins take over more of the b-sheet structure, allowing aggregation and self-propagation. This is followed by a process in which the b-sheet regions of the different molecules align themselves and interdigitate to form a dry interface. The final product is protofibrils, which are more resistant to amyloid degradation and can be formed through different mechanisms, one of which is amino acid substitution. In AL, certain amino acid substitutions are at specific positions in the variable region light chain and occur at a higher frequency compared with non-amyloidogenic Ig, causing destabilization of the light chain and increasing the possibility of fibrillogenesis. Similarly, in hereditary amyloidosis, genetic mutations with amino acid substitutions are the basis for the formation of amyloid fibrils.[12] The unstable proteins produced by amino acid substitutions allow the proteins to precipitate when stimulated by physical or chemical factors, such as local surface pH, electric fields, and hydration forces on cellular surfaces.[13]

Amyloids can deposit in many organs, and this tendency may depend on several factors, such as high local protein concentration, low pH, the presence of proteolytic processes, and the presence of fibril seeds. Amyloid deposits cause significant disruption of tissue architecture, which may underlie the mechanism of organ dysfunction. In addition, amyloidogenic precursor proteins, folding intermediates, and protofilaments have amyloid deposit-independent toxicity. Amyloid can regress over time by endogenous degradation.[3] Specific absorption light chains by mesangial cells underlie the dominant renal tropism and are an important step in amyloid formation in AL. Factors that may promote or inhibit amyloid deposition in the kidney include the negative charge and high glycosaminoglycan content of the glomerular basement membrane in the presence of certain proteases that can make the protein amyloidogenic.[14]

Mesangial cells are modified smooth muscle cells that express smooth muscle actin and muscle-specific actin. After interaction with light chains, the light chains routine is internalized and delivered to the mature lysosomal compartment, where primary amyloid fibrils are formed. During this process, mesangial cells undergo a change to a macrophage phenotype with a prominent lysosomal system, making them capable of processing light chains internalized amyloidogenic and fibril formation. Amyloid deposition within the mesangium then stimulates metalloproteinase activity, causing mesangial matrix damage, inhibits transforming growth factors impairing mesangial matrix repair, and increases apoptosis, ultimately leading to significant mesangial cell removal and replacement by amyloid deposits.[13]

The kidney is an organ that is often affected by AL, AA, and some familial amyloidosis. Kidney biopsy is a method that is often used to identify the disease. The risk of procedure-related bleeding as a result of vascular fragility in individuals with amyloidosis is expected. However, there is little evidence that bleeding rates are high after renal biopsy in these patients. Amyloid can be found anywhere in the kidney, but glomerular deposition usually predominates. By light microscopy, glomerular amyloid appears as an amorphous material in the mesangium and capillary loops. Substantial mesangial deposition can produce nodules that resemble lesions of diabetic nephropathy or light chain deposition disease (LCD). However, in amyloidosis, because the nodules are composed of amyloid protein rather than extracellular matrix, periodic acid-Schiff (PAS) weak staining. Amyloid deposition in the interstitial tubules results in tubular atrophy and interstitial fibrosis, and in a minority of patients, glomerular deposition is little or absent, and amyloid is confined to the interstitial tubules or blood vessels. Regardless of amyloid distribution, Congo red staining produces disease-defining birefringence under polarized light.[3]

Clinical appearance

The clinical presentation of patients with renal amyloidosis is determined by the type of amyloid, the location and amount of amyloid deposition within the kidney, and the extent of extrarenal involvement. The most common manifestation of amyloidosis kidney disease is proteinuria, which ranges from minimally nephrotic to massive, depending on the degree of glomerular involvement. AL amyloidosis commonly affects the glomerulus, and patients with Amyloidosis AL kidneys often show high levels of proteinuria, with >65% of patients suffering from nephrotic syndrome. Clinically, more than 75% of patients with amyloidosis kidneys present with peripheral edema. This is due to nephrotic syndrome, renal failure, heart failure, or a combination.[15,16]

Systemic amyloidosis of AL and AA commonly presents with nephrotic proteinuria associated with extensive glomerular amyloid deposition. Soft tissue involvement is common in AL Amyloidosis, with macroglossia and periorbital bruising being pathognomonic features of this disease. Macroglossia appears as painful dry sores on the tongue, increased tongue biting, and indentation of the teeth.[4]

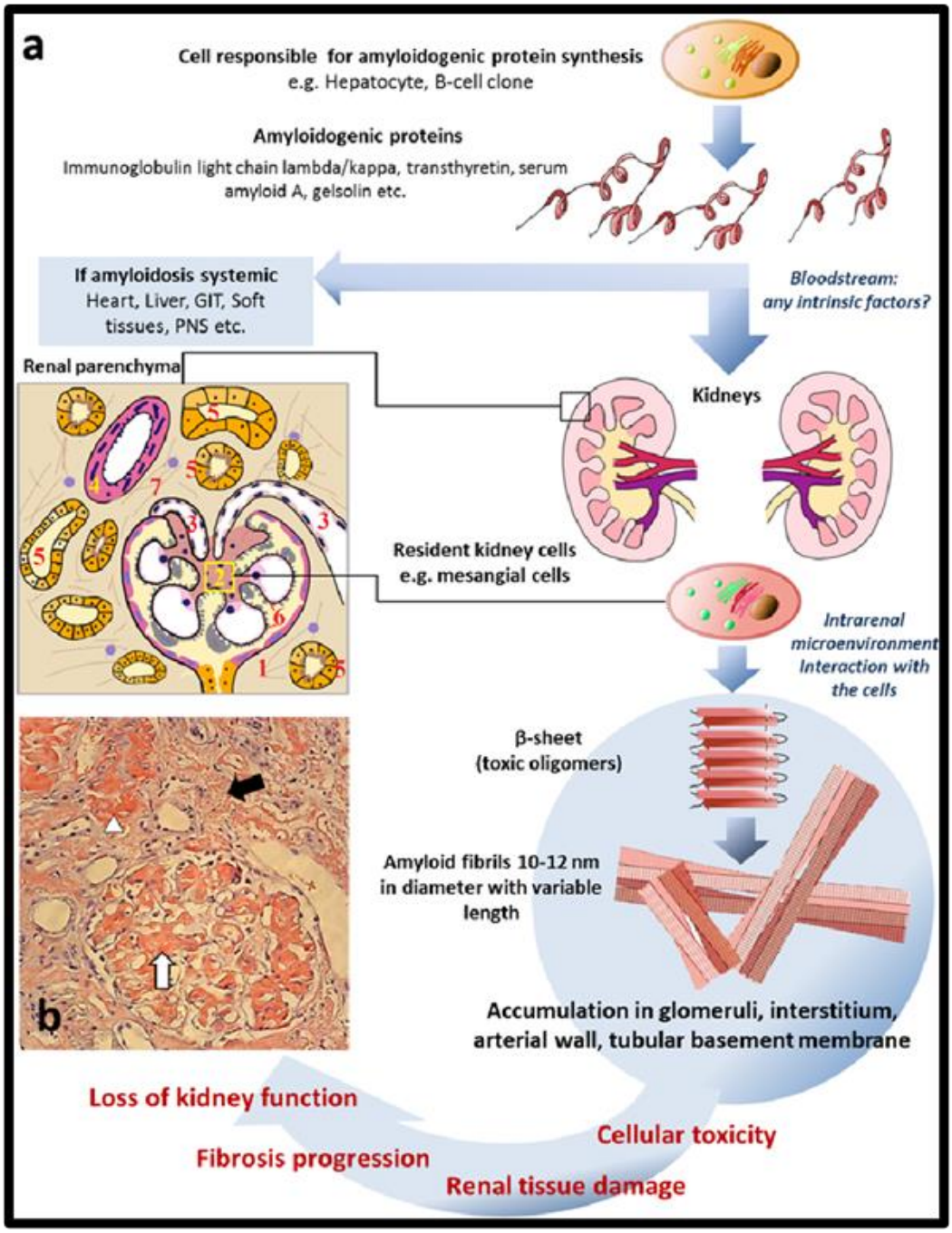

Figure 4. Pathogenesis of amyloidosis.[10]

Proteinuria and nephrotic syndrome

Proteinuria is the most common manifestation and is generally associated with glomerular amyloid deposition. For example, approximately 75% of patients with AL Amyloidosis (most of whom have predominant glomerular deposition) present with proteinuria, often accompanied by edema. The urine sediment is usually bland (reflecting the lack of glomerular inflammation), and the plasma creatinine concentration may be normal or only slightly elevated. End-stage renal disease (ESRD) develops in approximately 20% of those with nephrotic syndrome.[17]

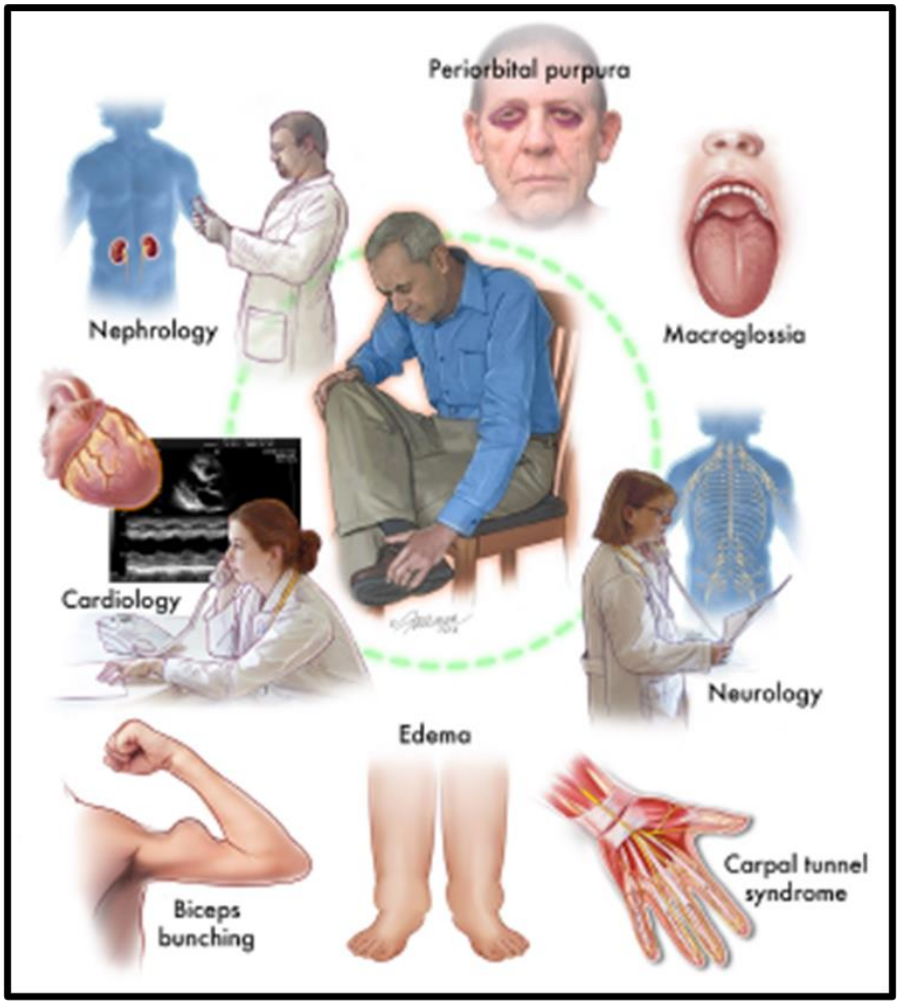

Figure 5. Clinical symptoms of amyloidosis.[9]

Slowly progressive CKD with little or no proteinuria

Slowly progressive chronic kidney disease (CKD) with little or no proteinuria is a common presentation of patients with amyloidosis AA who have amyloid deposits primarily confined to the blood vessels and tubulointerstitial areas. Impaired renal function without significant proteinuria is also a major manifestation of patients with predominant tubulointerstitial amyloid deposition, such as those with ALECT2, apolipoprotein AI (AApoAI) Amyloidosis associated with Leu75Pro mutations, or AApoAIV amyloidosis.[17]

Tubular dysfunction

Tubular dysfunction such as type 1 (distal) renal tubular acidosis or polyuria due to nephrogenic diabetes insipidus may be presenting features in patients with severe tubular deposition.[17]

Glomerulonephritis sabit

Crescent glomerulonephritis is a very rare presentation in patients with renal amyloidosis AA. Nearly all reported patients suffer from amyloidosis AA due to rheumatoid arthritis or its variants. A possible mechanism is the induced rupture of amyloid fibrils in the capillary loops, leading to fibrin entry into Bowman's chamber.[17]

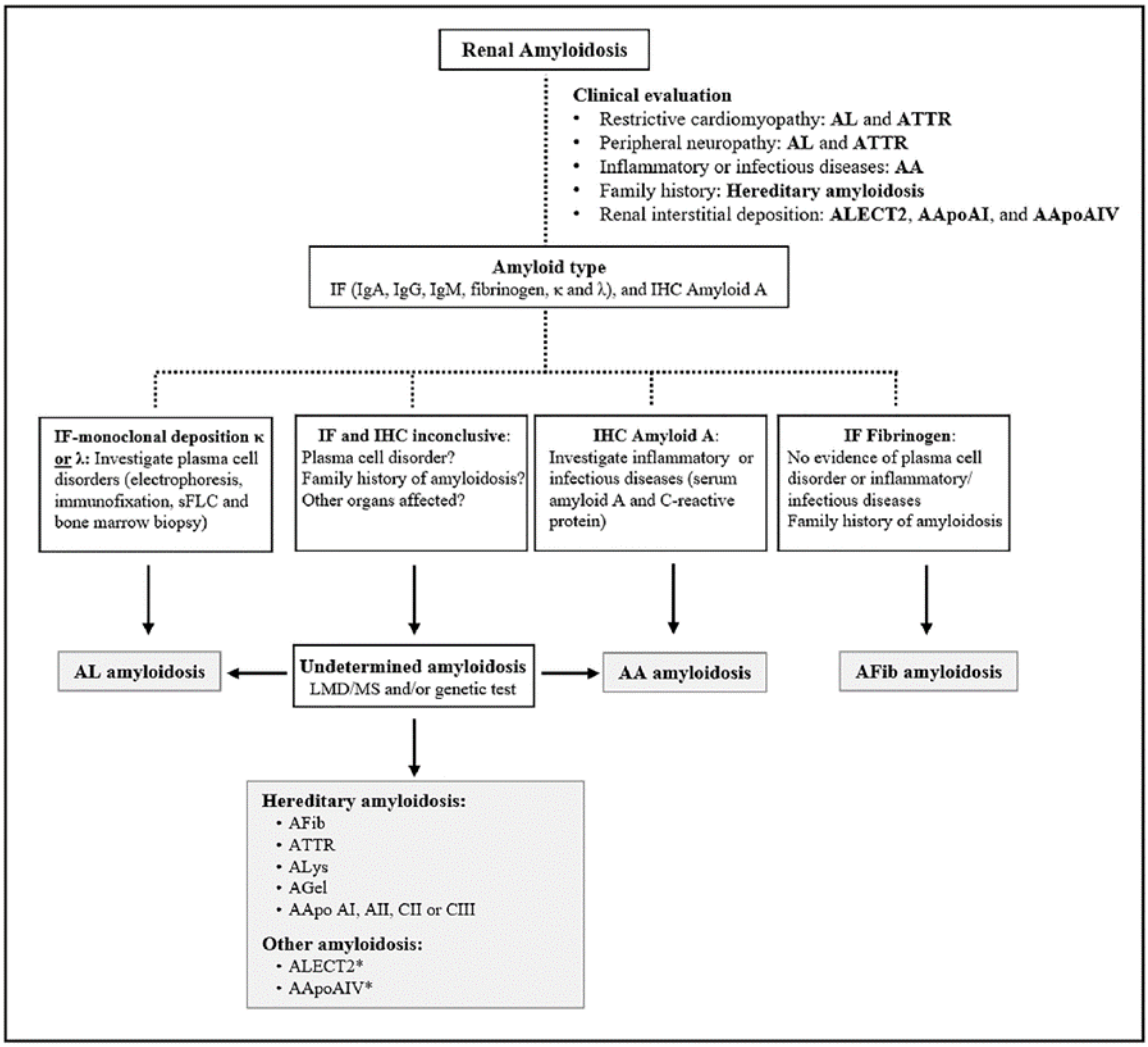

Figure 6. Chart of the clinical appearance of renal amyloidosis.[6]

Acute kidney injury

In rare cases, patients with AL amyloidosis may present with acute kidney injury due to intratubular cast amyloid nephropathy. In such patients, light chain immunoglobulins may precipitate to form intratubular casts similar to cast nephropathy light chain myeloma. However, these casts are congophilic and display fibrillar structures under the electron microscope.[17]

Histology and light microscopy

Positive histology is necessary for the diagnosis of amyloidosis, but a negative result does not rule out the presence of amyloidosis. In general, histology is a poor method for establishing the extent or distribution of amyloid because deposits can be patchy. The current diagnostic gold standard is the presence of apple green birefringence when a tissue biopsy is stained with Congo red viewed under polarized light. Biopsy is the gold standard of diagnosis, and serum amyloid P component scintigraphy can help determine the type and distribution of amyloid.[18]

Tissue biopsy should be used to confirm the diagnosis in all cases. Fat aspiration biopsies are less likely to cause serious bleeding compared with liver, kidney, or rectal biopsies. In patients with single organ involvement, biopsy of the clinically involved site is recommended because fat pad aspiration biopsy tends to be low in sensitivity for Amyloidosis in such patients.[19]

Kidney biopsy samples were immersed in paraffin and then stained with hematoxylin-eosin, periodic acid Schiff, periodic acid methenamine silver, and Congo red. At final diagnosis, all cases were confirmed to have amyloid fibrils by electron microscopy.[20] The diagnosis of amyloid is based on the finding, by light microscopic examination, of positive amorphous extracellular deposits Congo red, which shows characteristic dichroism and birefringence apple green under polarized light. Staining Congo red may be false negative if the tissue section is less than 5 µm thick. When possible, non-invasive biopsies of abdominal fat and minor salivary glands should be performed initially. Positive persistent Congo red after treatment of the biopsy sample with potassium permanganate was suggestive but not specific for AL amyloidosis. The presence of serum or urine paraproteins is also not sufficient to establish a diagnosis of AL amyloidosis due to the frequency of monoclonal gammopathies in patients over 50 years of age.[21]

With an electron microscope, amyloid appears as unbranched fibrils with a diameter of 8 to 10 nm. Fibrils are randomly arranged without any particular orientation in the mesangium, basement membrane, interstitium, and blood vessels. Immunoelectron microscopy can be used to determine the type of amyloid, but its availability is limited in research laboratories. The size of the fibrils distinguishes amyloidosis from other kidney diseases with organized Ig deposits. The fibrils of fibrillary glomerulonephritis and microtubule immunotactoid glomerulopathy usually have diameters of 15 to 20 and 30 to 60 nm, respectively. The fibrils of fibrillary glomerulonephrites, like amyloid, are arranged randomly, whereas the microtubules of immunotactoid glomerulopathy have an ordered, parallel orientation. The electron micrographic appearance of amyloid fibrils is quite typical; if present, the diagnosis of amyloidosis should continue to be considered even when Congo red staining is negative.[3]

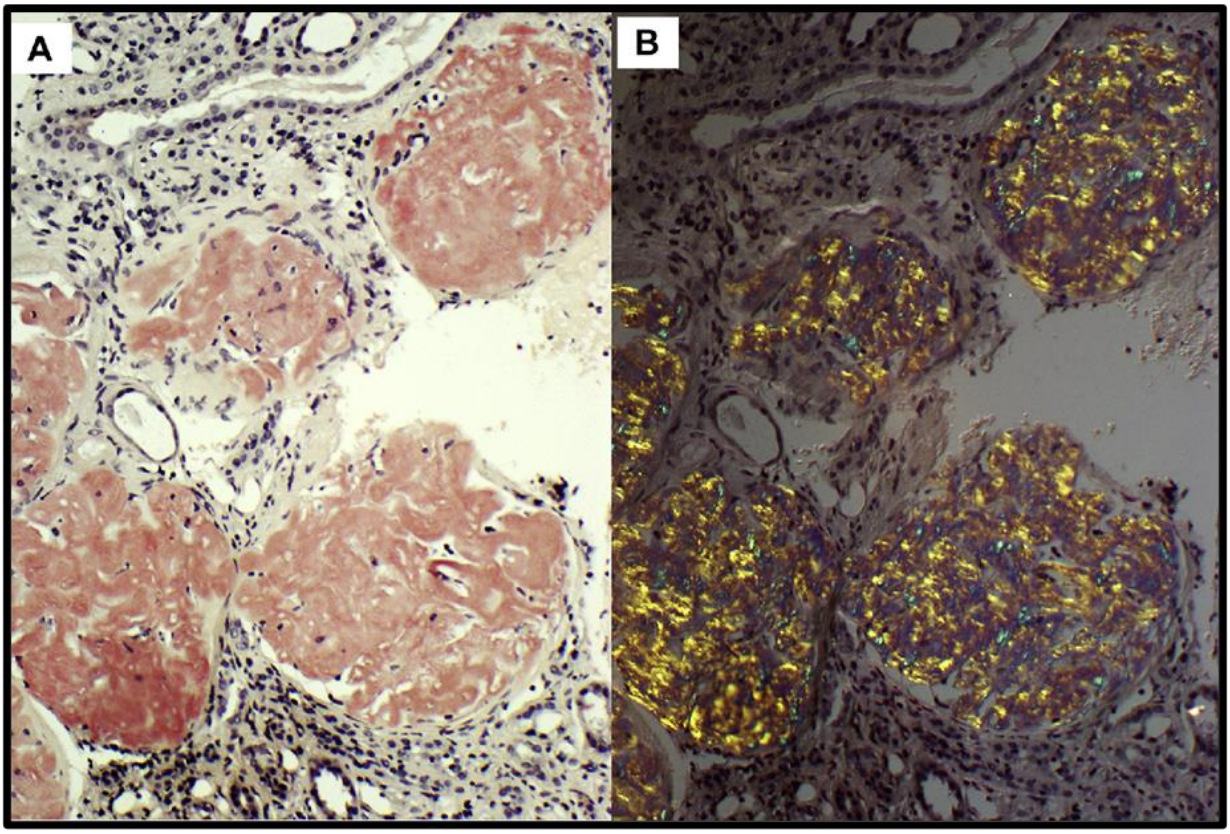

Figure 7. Glomerulus with amyloid: stained Congo red (A); viewed with a light microscope (B).[13]

Disease course and prognosis

The course and prognosis vary based on the type of amyloid and response to treatment, although progressive deterioration in renal function is expected in most forms of renal amyloidosis, although the rate of progression is influenced by a number of factors. Patients with AL renal amyloidosis tend to have a more rapid decline in renal function compared with other forms of amyloidosis, and ESRD occurs in approximately 25% of these patients.[22] Proteinuria >5 g/day and estimated glomerular filtration rate <50 mL/min were found to be the best independent predictors of ESRD. Renal response to therapy is highly correlated with hematologic response, and achievement of renal response is associated with improved renal and patient survival. In Amyloidosis AA, renal dysfunction is the most common clinical manifestation and is an important predictor of patient outcomes. In a study of 374 patients with Amyloidosis AA, the median survival from diagnosis was 133 months. Patients who achieved ESRD had a 2.97 times higher risk of death compared with those who did not. Risk factors for ESRD include a large amyloid load, a longer duration of inflammatory disease, and elevated serum creatinine. Tight control of inflammatory disease causes and reduction of amyloid deposition has been shown to lead to improved proteinuria and renal function.[15]

Disturbance of tissue structure by amyloid deposits is the mechanism underlying organ dysfunction in amyloidosis. The detrimental impact of amyloid on surrounding tissues is easily assessed from histological examination of kidneys that have extensive amyloid deposits. However, several observations suggest that amyloidogenic precursor proteins, fold intermediates, and protofilaments have toxicity independent of amyloid deposits and that this toxicity contributes to disease manifestations, as in Figure 9. The right-hand side illustrates that amyloid fibrils accumulate in the extracellular space, causing physical disturbances. and damage to surrounding tissue. The left side depicts alternative mechanisms of direct cellular toxicity by amyloidogenic precursor proteins, folded intermediates, aggregates, or fibrils. This toxicity can be mediated through interactions with cell surface receptors or through entry into cells. Findings supporting the latter mechanism include the lack of correlation between the amount of amyloid in tissue and organ dysfunction, the in vitro demonstration of direct toxicity of amyloidogenic precursor protein in cultured cells or tissue, the detection of amyloidogenic precursor protein in tissue in the absence of amyloid and the rapid improvement of markers of organ dysfunction after treatment-induced reduction in precursor protein production.[3]

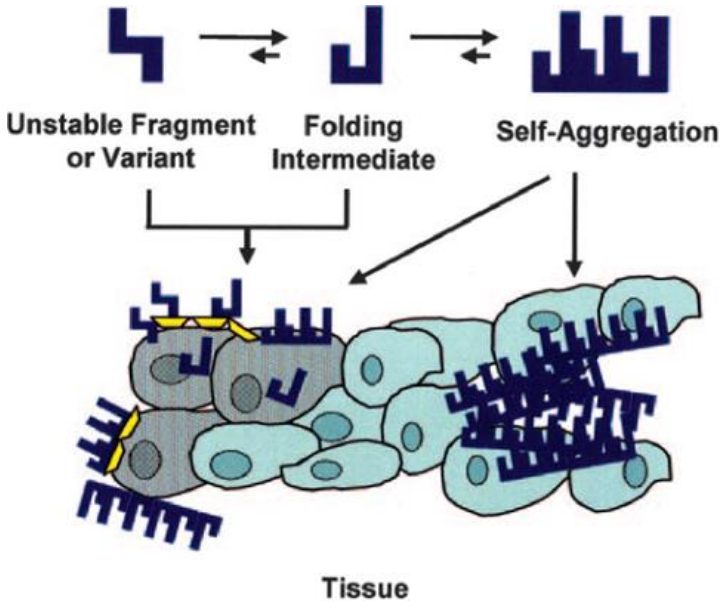

Figure 8. Mechanism of organ dysfunction in amyloidosis.[3]

Disease management

Treatment of amyloidosis is divided into two parts. The first stage is managing the symptoms experienced by the patient to improve comfort, quality and function of life, and prolong survival. The next part of treatment is to reduce or stabilize the amyloid protein to prevent the formation of amyloid deposits.[9] Without treatment, renal amyloidosis will eventually lead to end-stage renal disease (ESRD) or death in the majority of patients. Therapy for renal amyloidosis varies with the type of amyloid. Optimal management usually combines therapy targeting the underlying amyloid formation process and supportive management. The goals of treatment are to reduce the amyloid load, limit further kidney injury, and maintain or improve kidney function. Renal response was measured by changes in renal function (serum creatinine, estimated glomerular filtration rate) and proteinuria. In AL Amyloidosis, the success of treatment is determined by the hematological response and organ response. Renal response was defined as a 50% decrease in urinary protein excretion within 24 hours in the absence of 25% serum creatinine or creatinine clearance.[15] Treatment of systemic AL amyloidosis relies primarily on chemotherapy aimed at suppressing Ig LC (light chain) secreting plasma cell clones. AL amyloidosis results from a balance between amyloid deposition and clearance of deposits.[21]

Amyloidosis AA treatment targets chronic inflammatory or infectious conditions, thereby suppressing or reducing the production of the amyloid precursor serum protein amyloid A. In certain forms of amyloidosis hereditary renal in which the liver is the primary location of the precursor protein amyloid production (AFib and AApoAI), kidney transplantation earlier in the course of the disease should be considered.[15]

In general, dialysis outcomes among patients with AL Amyloidosis who require dialysis are not as good as those of patients with other kidney diseases who require dialysis. In previous studies, median survival ranged from 8 to 26 months. Subsequent studies have shown modest improvements in outcomes. For example, a UK study of 222 patients with AL Amyloidosis on dialysis reported a median survival of 39 months. Dialysis among patients with Amyloidosis AA requiring dialysis is generally poor although much of the data comes from older studies, for example in a retrospective study including 20 patients with Amyloidosis AA requiring dialysis, three patients (15%) died within a median of 32 months.[17]

The results of kidney transplantation treatment in AL Amyloidosis appear to be more favorable, especially in selected patients without other severe organ failure and who have a complete or excellent partial hematological response before transplantation. In AA Amyloidosis patients, treatment with kidney transplantation is better than dialysis.[17]

Supportive management Amyloidosis was systemic with cardiorenal involvement based on diuretics, perhaps angiotensin receptor blockers are poorly tolerated due to hypotension.[4] Supportive measures are common in all patients with amyloidosis. Renal management includes dietary sodium and protein restriction, blood pressure control, treatment of dyslipidemia, and, in selected patients, anticoagulation. Other aspects of therapy include diuretics to control edema and maintain adequate nutrition.[17]

Dietary salt and fluid restriction are important components of management of edema in these patients. Although use of loop diuretics initially causes substantial sodium loss, repeated doses do not result in a negative sodium balance. Dietary sodium restriction has been shown to increase the capacity of the distal tubule to transport sodium and chloride.[23]

2. Conclusion

Amyloidosis is a multisystemic disease that often affects the kidneys and manifests as nephrotic syndrome. AL amyloidosis remains the most common cause of renal amyloid. The most common clinical manifestations of renal amyloidosis are proteinuria with frequent nephrotic syndrome and progressive renal dysfunction. After clinical suspicion, the diagnosis should be confirmed by histological

examination using Congo red staining under polarized light, which produces positive birefringence. The gold standard for diagnosing kidney involvement is a kidney biopsy. In patients with amyloidosis kidneys, identifying monoclonal proteins by serum and urine protein electrophoresis and/or immunofixation is not sufficient to establish a diagnosis of AL amyloidosis. Treatment for Amyloidosis varies based on the pathogenic fibrils, the severity of the disease, and organ involvement. Management of renal amyloidosis varies with the type of amyloid and, as usual, combines therapy targeting the underlying amyloid process and supportive management.

Treatment of amyloidosis kidney disease can be complicated and often requires a multidisciplinary approach by an Oncologist, Nephrologist, and Cardiologist. Supportive therapy is also required in AL Amyloidosis with renal involvement. Patients with amyloidosis Kidneys that progress to end-stage renal disease can be treated with dialysis and, in certain patients, with kidney transplantation.

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