Clinical, biopsy, and mass spectrometry findings of renal gelsolin amyloidosis

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Gelsolin amyloidosis is a rare type of amyloidosis typically involving the cranial and peripheral nerves, but rarely the kidney. Here we report the clinical, kidney biopsy, and mass spectrometry findings in 12 cases of renal gelsolin amyloidosis. Of the 12 patients, five were men and seven were women with mean age at diagnosis of 63.8 years. Gelsolin amyloidosis was most common in Caucasians (six patients) and Asians (four patients), and included one each African-American and Hispanic patients. Nephrotic syndrome was the most common cause of biopsy, although most patients also had progressive loss of kidney function. Hematological and serological evaluation was negative in 11 patients, while one patient had a monoclonal gammopathy. The renal biopsy showed large amounts of pale eosinophilic Congo red–positive amyloid deposits typically restricted to the glomeruli. Immunofluorescence studies were negative for immunoglobulins in nine cases with three cases of smudgy glomerular staining for IgG. Electron microscopy showed mostly random arrangement of amyloid fibrils with focally parallel bundles/sheets of amyloid fibrils present. Laser microdissection of the amyloid deposits followed by mass spectrometry showed large spectra numbers for gelsolin, serum amyloid P component, and apolipoproteins E and AIV. Furthermore, the p. Asn211Lys gelsolin mutation on mass spectrometry studies was detected in three patients by mass spectrometry, which appears to represent a renal-limited form of gelsolin amyloidosis. Thus, renal gelsolin amyloidosis is seen in older patients, presents with nephrotic syndrome and progressive chronic kidney disease, and histologically exhibits glomerular involvement. The diagnosis can be confirmed by mass spectrometry studies.

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Gelsolin amyloidosis (AGel) is a rare form of amyloidosis that was first described in the Finnish population and is often labeled as familial amyloidosis of the Finnish type.[1] AGel amyloidosis is a type of hereditary systemic amyloidosis typically presenting as an autosomal dominant polyneuropathy syndrome.[2] AGel most commonly involves the cranial and peripheral nerves, resulting in progressive cranial neuropathy, corneal lattice dystrophy, and distal sensorimotor neuropathy.[1,3,4]

Although AGel amyloidosis predominantly involves the nerves, AGel amyloidosis has also been described in the skin, heart, and kidney. Renal involvement is rare and has mostly been documented in only a few case reports.[5–9] In this report, we present the clinical, renal biopsy, and mass spectrometry findings of 12 patients with renal AGel amyloidosis.

RESULTS

Clinical features

Twelve patients with renal AGel amyloidosis were included in the study. Renal AGel amyloidosis was present in both males (5 patients) and females (7 patients) (Table 1). In 11 patients, AGel amyloidosis was present in the native kidney, whereas AGel amyloidosis was detected in the allograft kidney of 1 patient (patient 5). A biopsy was not performed on the native kidney in the patient with AGel amyloidosis in the allograft kidney. The mean age at time of diagnosis was 63.8 years (range, 48–79 years). Six patients were Caucasian, 1 of whom had Finnish/Scottish ancestry, 2 of whom had German ancestry, and in the remaining 4, the ancestry was unknown; 4 patients were Asian, of whom 1 was Korean, 1 was Filipino, and in the remaining 2, the ancestry was unknown; 1 patient was African American, and 1 patient was Hispanic. Family history of kidney disease, including polyneuropathy, was present in 3 patients. Comorbid conditions were present in all patients and included hypertension, diabetes, gout, monoclonal gammopathy of undetermined significance, rheumatoid arthritis, smoking, and obesity.

The mean serum creatinine at presentation was 1.98 mg/dl (range, 0.5–3.8 mg/dl). All patients except 1 (patient 6) presented with moderate to severe proteinuria. The mean

Table 1 | Demographic, clinical, and histological characteristics of renal AGel patients

Patient	Age, yr	Sex	Ethnicity	Comorbidity	Serum Cr	Proteinuria (mg/24 hr)	Bone marrow genetics or family history	Glomerular/interstitial/vascular involvement	Electron microscopy, fibrils with organization[a]
1	55	M	Filipino	DM, HTN	2.0	8600	NA	+++/−/−	Present
2	61	F	African American	HTN	1.7	6000	NA	+++/−/−	NM
3	79	F	Scottish, Finnish	HTN	1.6	4450	Normal BM family history of p.Asp214Asn mutation	+++/+/−	NM
4	70	F	Asian	DM, HTN, renal artery stenosis	1.8	8600	Normal BM p.Asn211Lys mutation on MS	+++/−/−	NM
5	48	F	Hispanic	HTN, DM	2.9	2000	NA	++/−/−	Present
6	75	F	Caucasian	HTN, gout, RA, MGUS	3.8	133	Normal BM p.Gly194Arg mutation	+++/−/−	Present
7	50	F	Korean	DM	0.5	2000	No family history of kidney disease	+++/−/−	Present
8	67	M	German	Degenerative disc disease	1.1	6700	p.Asn211Lys mutation in 4 of 12 family members	+++/−/−	NM
9	61	M	German	HTN, DM, smoking, obesity	2.6	13,200	p.Asn211Lys mutation in 4 of 12 family members	+++/−/−	NM
10	59	F	Caucasian	HTN, osteoarthritis	1.8	3000	p.Asn211Lys mutation on MS, sister has kidney disease	+++/−/−	Present
11	68	M	Caucasian		1.0	Nephrotic syndrome	History of familial polyneuropathy	+++/−/−	Present
12	72	M	Asian	HTN	1.8	Nephrotic syndrome	p.Asn211Lys mutation on MS Family history of kidney disease	+++/−/−	NM

BM, bone marrow; Cr, creatinine (mg/dl); DM, diabetes mellitus; F, female; HTN, hypertension; MGUS, monoclonal gammopathy of undetermined significance; M, male; MS, mass spectrometry; NA, not available; RA, rheumatoid arthritis.

[a]Amyloid fibrils with parallel, wavy, storiform arrangement. NM fibrils with a wavy or storiform pattern were not mentioned in the report.

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