# Hereditary Fibrinogen A Amyloidosis (HaFib): A Rare Etiology of Nephrotic Syndrome and Acute Kidney Injury

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## BACKGROUND

Amyloidosis is a rare condition involving abnormal systemic protein deposition. It can be further categorized into various types including amyloid associated (AA), amyloid light chain (AL), Hereditary, Wild type and localized amyloidosis. Hereditary Fibrinogen A Alpha Amyloidosis (HaFib) is a form of hereditary amyloidosis which occurs due to a genetic mutation in fibrinogen resulting in abnormal fibrinogen production by the liver. HaFib is a systemic disease first characterized in 1993 in a Peruvian family[1].

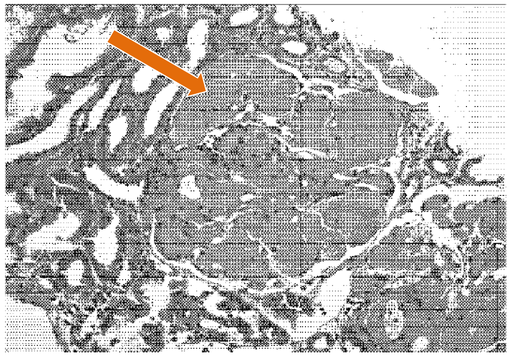
We present a patient with newly diagnosed nephrotic syndrome and cardiomyopathy in the setting of acute kidney injury (AKI) due to fibrinogen amyloidosis.

## CASE PRESENTATION

A 59 yo female was admitted with a chief complaint of shortness of breath and physical exam consistent with volume overload.

- a Cr of 1.3mg/dL two years prior
- Cr on admission was 2 mg/dL.
- On presentation, had AKI, new-onset cardiomyopathy, and atrial fibrillation.
- Labs revealed:
  - nephrotic range proteinuria (7 gm)
  - a mildly low C3
  - 2D-Echo revealing an EF of 40% with eccentric hypertrophy and Grade 1 diastolic dysfunction
  - SPEP, UPEP, FLC ratio, ANCA profile, C4, ANA, anti-ds-DNA, and MPO, PR3, Hep B, Hep C and HIV antibodies were normal
  - Renal ultrasound demonstrated bilateral echogenic kidneys 11 cm in diameter.

## PATHOLOGY



Hypocellular amorphus material

The renal biopsy

- 10/41 globally sclerotic glomeruli with massive infiltration of the mesangium and glomerular capillaries by amorphous pauci-cellular
- Periodic Acid-Schiff Stain slightly pale
- Jones Methenamine Silver negative material
- Congo red revealed positive staining and green birefringence upon polarization.
- Immunostaining for AA amyloid was negative
- Electron microscopy randomly oriented fibrils measuring 9nm on average with foot process effacement involving 75% of the glomerular capillary surface
- The amyloid protein was identified as being Fibrinogen alpha.

## CASE ON FOLLOW UP

- On follow up she was diagnosed with stage 4 CKD with a baseline Cr of 2-2.5mg/dL and has been started on an ACEI for proteinuria reduction.
- To exclude infiltrative cardiomyopathy, she is undergoing further cardiac evaluation.
- She is also being worked up for eventual liver / liver + kidney transplant as this is currently the only promising curative treatment for this condition.
- Eventually, the patient shared a strong family history of cardiac and renal disease.

## DISCUSSION

1. HaFib is the leading cause of hereditary renal amyloidosis associated with nephrotic syndrome in the United States. It is an autosomal dominant mutation in the fibrinogen A alpha chain gene. It presents with proteinuria and features a progressive decline in kidney function leading to End Stage Renal Disease (ESRD) within 5 years of diagnosis[2].

2. Stangou et al have reported benefits of preemptive solitary liver transplantation early in the course of amyloid nephropathy to prevent hemodialysis and kidney transplantation[3]. Solitary Renal transplantation is associated with recurrence of amyloid in the graft with a resultant loss of the transplanted kidney after a median of 6.7 years[3].

3. This case illustrates the need for thorough history taking including detailed family history in evaluating patients with nephrotic syndrome and AKI.

## REFERENCES

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3. A.J.Stangou, N.R.Banner et al, Hereditary fibrinogen A alpha chain amyloidosis: phenotypic characterization of a systemic disease and the role of liver transplantation”, Blood, vol 115, April 15, 2010, number 15, pp 2998- 3007.

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