Central Asian Journal of Nephrology
(eISSN 3105-4145)

Case Report

AA-Amyloidosis in an Adolescent with Familial Mediterranean Fever: A Case Report

Saltanat Rakhimzhanova[1], Galiya Shaimardanova[2], Aigerim Smagulova[2], Aidana Nalibek[1]

[1]*Department of Nephrology and Dialysis, University Medical Center, Astana, Kazakhstan*
[2]*Department of Pathomorphology, National Scientific Medical Center, Astana, Kazakhstan*

Received: October 8, 2025
Accepted: October 19, 2025

Corresponding author's email:

nalibekaidana@gmail.com

Abstract:

Familial Mediterranean Fever (FMF) is an autosomal recessive autoinflammatory disorder caused by mutations in the MEFV gene. It is most common among populations from the Eastern Mediterranean region, including Turks, Armenians, Arabs, and Sephardic Jews. One of the most serious complications of FMF is AA amyloidosis, which develops as a result of chronic inflammation and the deposition of serum amyloid A protein. AA amyloidosis frequently affects the kidneys, leading to nephrotic syndrome and chronic kidney disease.

We report a case of a 17-year-old Turkish male presenting with recurrent episodes of fever, joint pain, periodic skin rashes, and intermittent hypertension. Laboratory evaluation revealed nephrotic-range proteinuria, hypoalbuminemia, low serum IgG, and elevated inflammatory markers. Renal biopsy confirmed AA amyloidosis with moderate interstitial lymphocytic infiltration and mild fibrosis. Genetic testing identified a homozygous pathogenic variant in exon 10 of the MEFV gene (p.Met694Val), previously reported and strongly associated with FMF.

This case highlights the rarity of such presentations and emphasizes the importance of early diagnosis of FMF complicated by AA amyloidosis. The patient remains on colchicine therapy with careful monitoring for potential complications; corticosteroids were gradually tapered following confirmation of amyloidosis, with supportive and symptomatic management continued.

Keywords: Familial Mediterranean Fever; Secondary amyloidosis (AA); MEFV protein; nephrotic syndrome; renal biopsy

Introduction

AA amyloidosis is a systemic disease characterized by extracellular deposition of fibrils derived from serum amyloid A protein, primarily affecting the kidneys and leading to nephrotic syndrome and renal failure (1,2). Familial Mediterranean fever (FMF) is the most common hereditary autoinflammatory disease and the leading cause of AA amyloidosis in many regions (3-5). It is caused by mutations in the MEFV gene, particularly in exon 10, such as the p.Met694Val variant, associated with severe disease and amyloid risk (6,7).

Although FMF predominantly affects populations around the Mediterranean basin-Turks, Armenians, Arabs, and Jews-cases have been increasingly reported outside endemic areas (3,4). In Central Asia, including Kazakhstan, FMF is rarely diagnosed, often due to limited awareness and the nonspecific presentation of early symptoms. Studies indicate that initiating colchicine therapy early in FMF patients can lower the risk of developing amyloidosis, even before any signs of kidney complications appear (8).

Renal biopsy remains the cornerstone for diagnosing AA amyloidosis, confirming amyloid type, and guiding management (9). Early detection and targeted anti-inflammatory therapy, primarily colchicine, have been proven to reduce amyloid deposition and improve prognosis (10). Our case represents one of the first documented biopsy-proven FMF-related AA amyloidosis cases in Kazakhstan, emphasizing the diagnostic challenges and the necessity of early morphological verification in atypical clinical scenarios.

Case Report

The patient, a 17-year-old male of Turkish ethnicity, was admitted to the nephrology department with complaints of lower limb edema, decreased urine output (diuresis), knee joint pain with restricted mobility, and limping. The complaints were accompanied by intermittent fever reaching 38–40 °C. During febrile episodes, hemorrhagic rashes and occasional purpuric lesions on the skin of the shins and thighs were noted, which disappeared upon normalization of temperature. Episodes of arterial hypertension (AH) alternating with hypotension were also recorded. On physical examination: height-168.5 cm, body weight -46.5 kg, body temperature -36.4 °C, edema of the shins, urine output (diuresis)-up to 2000 ml/day, gross hematuria (macroscopic blood in urine) was not observed. Laboratory tests at admission: hemoglobin (Hb) -107 g/dL, erythrocyte sedimentation rate (ESR) -57 mm/h, C-reactive protein (CRP)- 33.9 mg/L, urea -4.2 mmol/L, creatinine (Cr) -63.9 μmol/L, albumin -17.6 g/L, total protein -43.0 g/L. Immunogram: immunoglobulin M (IgM) -2.04 g/L, immunoglobulin G (IgG) - 3.99 g/L, immunoglobulin A (IgA) -1.42 g/L, rheumatoid factor (RF) -7.5 IU/mL. Immunological markers: antinuclear antibodies (ANA) negative (1:80), anticardiolipin antibodies (IgG, IgM) within normal range, anti-double-stranded DNA antibodies (anti-dsDNA), extractable nuclear antigens (ENA), anti-neutrophil cytoplasmic antibodies (ANCA), anti-glomerular basement membrane antibodies (anti-GBM) — negative. QuantiFERON test and GeneXpert were negative. Blood and urine cultures showed no growth. Urinalysis (UA) revealed proteinuria of 4.4 g/L. Renal ultrasound: right kidney — 123 × 49 mm, parenchyma 18 mm; left kidney — 129 × 55 mm, parenchyma 8 mm. X-ray of the knee joints: no bone-destructive changes, signs of arthritis. The patient was preliminarily diagnosed with primary steroid-resistant nephrotic syndrome of high activity. However, during hospitalization, a single episode of gross hematuria and episodes of arterial hypertension complicated the diagnostic process. Genetic analysis prior to renal biopsy results revealed a pathogenic homozygous variant MEFV p.M694V (rs61752717), typical for autosomal recessive familial Mediterranean fever (FMF). Additionally, a heterozygous variant of uncertain significance, LAMA5 p.His2445Tyr (rs200433384), was identified. Renal biopsy results showed morphological features of amyloid nephrosis with mild fibrosis and focal moderate lymphocytic infiltration in the interstitial tissue. All nine glomeruli contained massive extracellular amyloid deposits, moderate mesangial proliferation, thickening and lobularity of the basement membrane, and connective tissue adhesions. In the tubular epithelium — hyaline-droplet and hydropic degeneration, lipid inclusions, erythrocytes. Amyloid deposits were also present in the stroma and medium- to small-caliber vessels (Figure 1). Masson's trichrome histochemical staining demonstrated amyloid protein masses in all glomeruli, stained orange-blue (Figure 2). Congo red staining for amyloid was positive in six glomeruli, on the tubular basement membrane, stroma, and vessels, appearing orange-brown (Figure 3). AA amyloidosis of the kidneys on the background of autosomal recessive FMF was confirmed. Before renal biopsy results, treatment was initiated for nephrotic syndrome, single gross hematuria, and arterial hypertension: hydroxychloroquine (5 mg/kg, 300 mg/day), pulse therapy with methylprednisolone (750 mg × 3), followed by oral administration of 48 mg/day, and anakinra (100 mg × 2). Symptomatic therapy included albumin, immunoglobulin, calcium carbonate, diuretics, and antihypertensive drugs. After confirmation of AA amyloidosis and genetic analysis, glucocorticoids were gradually discontinued, and colchicine therapy (3 mg/day) was continued. After 2 months, the patient's condition: estimated glomerular filtration rate (eGFR) -100 mL/min, CRP decreased to 5.68 mg/L, albumin -31.82 g/L, total protein -52.24 g/L with ongoing replacement therapy. Clinical Course Table – see (Figure 4).

Figure 1. Immunofluorescence: Weak lambda light chain fluorescence observed in glomerular capillary loops, along the basement membrane, and in tubular epithelium. ×400.

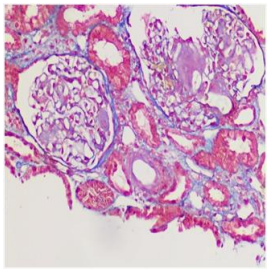

Figure 2. Segmental amyloid deposits in glomerular capillary loops and vascular walls, stained bluish-pink. Masson's trichrome staining, ×100.

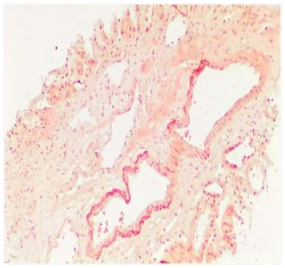

Figure 3. Pathological protein deposition in vascular walls showing orange-red coloration. Congo red staining for amyloid, ×400.

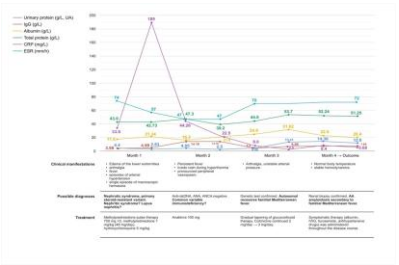

Figure 4. Clinical course of the patient during hospitalization. ESR – erythrocyte sedimentation rate (mm/h), CRP – C-reactive protein (mg/L), Total protein – total protein (g/L), Albumin – albumin (g/L), IgG – immunoglobulin G (g/L), Urinary protein (UA) – proteinuria in urinalysis (g/L), Anti-dsDNA – antibodies to double-stranded DNA, ANA – antinuclear antibodies, ANCA – antineutrophil cytoplasmic antibodies, IVIG – intravenous immunoglobulin.

Discussion

The goal of this case report is to underscore the clinical importance of recognizing FMF-related AA amyloidosis early, especially in regions where the disease is not endemic (1). Persistent subclinical inflammation due to unrecognized FMF can lead to irreversible renal damage (2). Early histopathological confirmation through renal biopsy enables appropriate treatment and prognosis assessment (1).

Historical cohorts have demonstrated that uncontrolled FMF with elevated SAA levels inevitably progresses to AA amyloidosis if untreated (5). Our diagnostic approach combined clinical symptoms, biochemical findings, and genetic testing with renal histology—aligning with recommendations from Ozen et al. and Lachmann et al. (5). The Congo red staining with characteristic apple-green birefringence under polarized light, and immunofluorescence confirming AA-type deposits, established the diagnosis (9).

Renal biopsy provided crucial diagnostic clarity by differentiating amyloidosis from other glomerulopathies, particularly in patients presenting with nephrotic-range proteinuria and hypertension (9). This morphological confirmation directly impacted clinical decisions—allowing de-escalation of glucocorticoids and continuation of colchicine therapy (10).

Colchicine remains the cornerstone of FMF therapy, preventing inflammatory attacks and amyloid deposition (10,11). In colchicine-resistant or intolerant patients, IL-1 inhibitors such as anakinra or canakinumab have shown efficacy in reducing inflammation and stabilizing renal function (11,12). Our patient responded well to colchicine monotherapy, maintaining remission and stable renal function without requiring biologics, consistent with published outcomes (13).

Compared with cases from endemic regions, this patient's delayed diagnosis and atypical presentation in Kazakhstan underline the geographic gap in awareness. Similar cases described by Yamada et al. (3) and Demirkaya et al. (5) also reported amyloidosis as the first clinical manifestation of FMF, reinforcing the need for genetic and histological evaluation in atypical nephrotic syndromes.

We recommend that clinicians in Central Asia include FMF in the differential diagnosis of unexplained nephrotic syndrome and hypertension in young patients. Early genetic testing and renal biopsy are critical for preventing irreversible organ damage (9). Close monitoring of SAA levels is also advised to evaluate inflammatory control (9,10).

Conclusion

This case highlights a rare instance of FMF-associated AA amyloidosis in Kazakhstan, demonstrating the vital role of early histological verification, genetic testing, and anti-inflammatory management. Colchicine remains the first-line therapy, while IL-1 blockade offers an option for refractory cases. Kidney transplantation outcomes in FMF-related amyloidosis remain insufficiently studied and warrant further investigation (13).

Disclosures: There is no conflict of interest for all authors.

Acknowledgments: None.

Funding: None.

Ethics approval: Not applicable.

References

1. Mirioglu S, Uludag O, Hurdogan O, Kumru G, Berke., et al. AA Amyloidosis: A Contemporary View. *Curr Rheumatol Rep*. 2024;26:248–259. **DOI**: 10.1007/s11926-024-01147-8
2. Bektas M, Koca N, Oguz E, Sari S, Dagci G., et al. Characteristics and course of patients with AA amyloidosis. *Rheumatology (Oxford)*. 2024;63(2):319–328. DOI: 10.1093/rheumatology/kead465
3. Yamada S, Parada X, Pasala S, Anumolu R, Alenizi S. AA amyloidosis unveiling familial Mediterranean fever in an atypical presentation. *J Am Soc Nephrol*. 2024;35:837–846. **DOI:** 10.1681/ASN.20241sjr2vxm
4. Ozeri DJ, Bar D, Safran BS, Druyan A, Kukuy OL, et al. Renal outcomes and survival in amyloidosis associated with FMF. *Semin Arthritis Rheum*. 2025;10:1035–1048. **DOI**: 10.1016/j.semarthrit.2025.152642
5. Ozen S, Demirkaya E, Erer B, Livneh A, Ben-Chetrit E, et al. Familial Mediterranean fever: a comprehensive review. *Ann Rheum Dis*. 2016;75(4):644–51. **DOI:** 10.1136/annrheumdis-2015-208690
6. Lachmann HJ, Goodman HJ, Gilbertson JA, Gallimore JR, Sabin CA, et al. Natural history and outcome in systemic AA amyloidosis. *N Engl J Med*. 2007;356:2361–2371. **DOI:** 10.1056/NEJMoa070265
7. GeneReviews®. Familial Mediterranean Fever. NCBI Bookshelf. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1226/.
8. Yin X, Tian F, Wu B, Xu T. Interventions for reducing inflammation in FMF: systematic review. *Cochrane Database Syst Rev*. 2022;CD013456. **DOI:** 10.1002/14651858.CD010893.pub4
9. Lancieri M, Bustaffa M, Palmeri S, Prigione I, Penco F, et al. An Update on Familial Mediterranean Fever. *Int J Mol Sci*. 2023;24(11):9584. **DOI:** 10.3390/ijms24119584
10. Mukhin NA, Kozlovskaya LV, Bogdanova MV, Rameev VV, Moiseev SV, Simonyan AKh. Predictors of AA amyloidosis in familial Mediterranean fever. *Rheumatol Int*. 2015;17:238. **DOI**: 10.1007/s00296-014-3205-x
11. Hosman IS, Kos I, Lamot L. Serum Amyloid A in Inflammatory Rheumatic Diseases. *Front Immunol*. 2021;11:631299. **DOI:** 10.3389/fimmu.2020.631299
12. Biederman LE, Dasgupta AD, Dreyfus DE, Nadasdy T, Satoskar AA, Brodsky SV. Kidney Biopsy Corner: Amyloidosis. *Glomerular Dis*. 2023;3(1):165-177. **DOI:** 10.1159/000533195
13. StatPearls. Familial Mediterranean Fever. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK570556/.