Massive Proteinuria and Acute Glomerulonephritis Picture in a Patient With Familial Mediterranean Fever and E148Q Mutation

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Familial Mediterranean fever (FMF) is an inherited auto-inflammatory disorder. Secondary AA amyloidosis is the most devastating complication of FMF. Nonamyloid renal involvements have also been reported in association with FMF, including vasculitis, focal and diffuse glomerulonephritis, and IgA nephropathy. We describe a patient with FMF and E148Q mutation who presented with massive proteinuria, elevated serum creatinine level, and acute glomerulonephritis picture. Disease remission was achieved after treatment with corticosteroids and colchicine.
Immunofluorescent staining was negative for IgA, IgM, IgG, C3, and C4 deposit. Congo red staining was negative. Analysis of the MEFV gene for FMF showed heterozygous mutation for E148Q mutation. The patient was of northwest Iranian origin from Azerbaijan.

She received 2 days of methylprednisolone pulse, 500 mg/d, followed by a tapering dose of prednisolone, 1 mg/kg, for 1 month and continuing dose of colchicine, 0.5 mg/d. After 6 months, proteinuria decreased to 1100 mg/d and kidney function returned to normal (serum creatinine level, 1.0 mg/dL), while she was on colchicine and angiotensin-converting enzyme inhibitor and angiotensin receptor antagonist therapies. Two years after treatment, her 24-hour protein excretion was 200 mg/dL, serum creatinine level was 1.2 mg/dL, and she did not have any abdominal pain episode during this period.

**DISCUSSION**

Late onset attacks of abdominal pain that disappeared after colchicine initiation, heterozygous mutation of E148Q, massive proteinuria, and acute glomerulonephritis-like picture in biopsy without any evidence of infectious etiology, all were an unusual combination in our patient. Nonamyloid kidney disease should be considered in the differential diagnosis of renal involvements in patients with FMF. In a study of 15 patients with a long-standing history of FMF and renal involvement, 7 patients had amyloidosis and 6 patients had mesangial proliferative glomerulonephritis. Immunofluorescent studies disclosed mesangial IgA deposits in 3 of them and IgM mesangial deposits in another 3 patients with mesangial proliferation. Two patients out of these 15 patients presented with rapidly progressive glomerulonephritis.7

Infectious-related glomerulonephritis was our first consideration, but we did not find any clinical sign of infection, since serum complement levels were normal and there was no C3 deposit on immunoflurescent microscopy.8 Because of increased inflammatory response immunologic glomerular injury may occur more frequently in patients with FMF.8 Mutated pyrin associates with uncontrolled inflammation through interleukin-1b and nuclear factor kappa-light-chain-enhancer of activated B cells activation.9,10 Whether or not E148Q mutation directs these inflammatory conditions toward the kidney or not needs future investigation.

In a report from Iranian Azeri Turkish patients, the most common mutation in FMF patients were p.M694V (42.4%), followed by p.V726A (17%), p.E148Q (16.2%), and p.M680I (c.2040G>C; 15.2%).4 In a study of 44 patients with E148Q mutation, 1 patient had rapidly progressive glomerulonephritis course.11 In another report, E148Q mutation presented with proteinuria and mesangial proliferative glomerulonephritis.11 It seems that E148Q mutation have heterogeneous clinical presentations. Other genetic modifiers may link to E148Q-associated clinical symptoms. In our patient, there was a discrepancy between clinical and pathologic findings.13,14 Increased inflammatory response may facilitate immunologic glomerular injury. Whether FMF should be considered in
the differential diagnosis of idiopathic meningeal proliferative glomerulonephritis in FMF endemic region needs future investigation.14

CONFLICT OF INTEREST
None declared.

REFERENCES


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