Taylor & Francis
Taylor & Francis Group

RENAL FAILURE

Renal Failure

ISSN: 0886-022X (Print) 1525-6049 (Online) Journal homepage: informahealthcare.com/journals/irnf20

Familial Mediterranean fever and membranous glomerulonephritis: report of a case

Mevlut Ceri, Selman Unverdi, Mustafa Altay, Hatice Unverdi, Arzu Ensari & Murat Duranay

To cite this article: Mevlut Ceri, Selman Unverdi, Mustafa Altay, Hatice Unverdi, Arzu Ensari & Murat Duranay (2010) Familial Mediterranean fever and membranous glomerulonephritis: report of a case, Renal Failure, 32:3, 401-403, DOI: 10.3109/08860221003640090

To link to this article: https://doi.org/10.3109/08860221003640090

Published online: 06 Apr 2010.

Renal Failure, 32, 401–403, 2010

ISSN: 0886-022X print / 1525-6049 online
DOI: 10.3109/08860221003640090

informa
healthcare

CASE REPORT

Familial Mediterranean fever and membranous glomerulonephritis: report of a case

Mevlut Ceri[1], Selman Unverdi[1], Mustafa Altay[2], Hatice Unverdi[3], Arzu Ensari[3] and Murat Duranay[1]

[1] *Department of Nephrology, Ankara Education and Research Hospital, Ankara, Turkey*

[2] *Department of Internal Medicine, Ankara Education and Research Hospital, Ankara, Turkey*

[3] *Department of Pathology, Faculty of Medicine, Ankara University, Ankara, Turkey*

ABSTRACT

Familial Mediterranean fever (FMF) is an autosomal recessive genetic disease characterized by recurrent attacks of fever and painful episodes of sterile polyserositis. Kidney involvement may occur as a result of secondary amyloidosis during the course of FMF. Previously, different types of glomerulopathies such as IgM and IgA nephropathy, crescentic glomerulonephritis, diffuse proliferative glomerulonephritis, minimal change disease, and membranoproliferative glomerulonephritis were rarely reported. We herein represent a first case of membranous glomerulonephritis who had complete remission with colchicine treatment in the course of familial Mediterranean fever.

Keywords: familial Mediterranean fever; kidney involvement; membranous glomerulonephritis; colchicine; complete remission

Received 10 August 2009; accepted 11 January 2010
Correspondence: Dr. Selman Unverdi, Department of Internal Medicine, Ankara Education and Research Hospital, Oğuzlar Mah. Osmanli Cad. 22/6, Balgat, Ankara, Turkey; tel: +90 312 5953194; fax: +90 312 5953302; E-mail: selmanunverdi@yahoo.com

INTRODUCTION

Familial Mediterranean fever (FMF) is an autosomal recessive genetic disease affecting mainly Turks, non-Ashkenazi Jews, Armenians, and Arabs. It is characterized by recurrent attacks of fever (38–40°C) and painful episodes of sterile polyserositis, typically involving the peritoneum, pleura, and synovia and less frequently rash, described as erysipelas-like erythema.[1,2] Mediterranean fever gene (MEFV), the gene responsible for the disease, mutation is localized on the short arm of chromosome 16 and encodes a 781-amino acid protein known as pyrin or marenostrin.[3] The MEFV transcript that is expressed in granulocytes plays an essential role in the inflammatory response.[4] Currently, more than 50 gene variants associated with a pathologic phenotype are known and variant forms of pyrin/marenostrin lead to inappropriate triggering of neutrophil activation.[5]

Renal involvement in FMF, which is usually dependent on secondary AA amyloidosis, may in some untreated patients lead to kidney failure and other organ damage. IgM nephropathy, IgA nephropathy, crescentic rapidly progressive glomerulonephritis, diffuses proliferative glomerulonephritis, minimal change disease, and membranoproliferative glomerulonephritis have also been reported,[6–10] but not membranous glomerulonephritis.

We describe an FMF patient who presented with persistent proteinuria and in whom kidney biopsy revealed membranous glomerulonephritis with no evidence of amyloidosis. Remission of her disease was observed while having taken only colchicine treatment during 1 year.

CASE REPORT

A 42-year-old female was admitted in our hospital because of proteinuria which was detected by routine urine analysis in April 2006. The patient had been diagnosed with FMF 10 years previously as a result of fever and severe abdominal pain attacks. His episodes of abdominal pain and fever, which began at age 30, subsided spontaneously within 1–3 days. The family history was negative for renal disease and FMF. Colchicine treatment had been initiated, but the patient gave up that treatment after a while. While the patient's blood pressure was 130/80 mmHg, she was taking telmisartan 80 mg/day. The remainder of the

physical examination was normal. Blood tests showed hemoglobin 13.3 g/dL, hematocrit 37.6%, white blood cells 11.800/mm^3, platelets 401.000/mm^3, erythrocyte sedimentation rate 49 mm/h, creatinine 0.74 mg/dL, urea 20 mg/dL, protein 7.4 g/dL, albumin 3.71 g/dL, serum glutamic oxaloacetic transaminase (SGOT) 18 UI/L, serum glutamic pyruvic transaminase (SGPT) 9 UI/L, triglycerides 383 mg/dL, total cholesterol 292 mg/dL, and low-density lipoprotein cholesterol 139 mg/dL. Urinalysis revealed a pH of 5 and urine density of 1010, and microscopically there were 3–4 erythrocytes, 2–3 leukocytes/high-power fields, and no cast/field in the urinary sediment. A 24-h urine collection revealed 2561 mg proteinuria/day, and creatinine clearance was 91 mL/1.73 m^2 per minute. Both throat and urine cultures were negative. Serologic tests for hepatitis B/C, antinuclear antibodies, anti-ds DNA, fibrinogen rheumatoid factor, serum immunoglobulins G, M, A, and complement were all normal.

Percutaneous kidney biopsy was performed because of continued proteinuria. Renal biopsy revealed typical membranous glomerulonephritis.

MEFV analysis showed M680 I/V726, a heterozygous mutation, confirming the diagnosis of FMF, and colchicine treatment was resumed (1.5 mg/day p.o.). After taking regular colchicine treatment, the patient had no fever and abdominal pain attacks. After 6 months proteinuria decreased by less than 50%. The following year the patient's proteinuria was 257 mg/day, creatinine 0.9 mg/dL, and creatinine clearance was 78.5 mL/1.73 m^2 per minute. There was no significant proteinuria change and creatinine clearance after the following 2 years.

DISCUSSION

Although many patients with FMF and glomerulonephritis have been documented in the literature, this is the first case of coexistence of membranous glomerulonephritis in patients with FMF described to our knowledge. Additionally, proteinuria resolved while on colchicine therapy.

Immunological mechanisms play important roles in the pathogenesis of FMF. MEFV encodes pyrin, which is expressed in mature neutrophils, and plays an essential role in the pressure of inflammation.[4] Adversely, mutated pyrin associates with uncontrolled inflammation through interleukin-1β (IL-1β) and nuclear factor kappa B (NF-κB) activation, resulting in upregulation of inflammatory cytokine pathways.[11]

It was reported that the patients with FMF are prone to exhibit a variety of glomerular disease other than amyloidosis. Said et al. reported the existence of mesangial IgA deposits in two patients with FMF displaying proteinuria and microscopic hematuria during their febrile attacks.[7] Nonamyloidotic renal involvement in the form of diffuse proliferative glomerulonephritis was reported by Tekin et al. in three patients with FMF-associated vasculitis.[9] Akpolat et al. described a 25-year-old patient, whose proteinuria remitted partially with prednisolone and azathioprine, who had membranoproliferative glomerulonephritis with FMF.[12] Immune complexes are exhibited in 50% of FMF patients.[6] IgM, IgA, and C3 deposits found in the mesangium in previously reported cases[3,6,11] are supportive of immunologic mechanism. Similarly, IgG and C3 deposits have been determined in the glomerular basement membrane of the present case.

Colchicine binds to β-tubulin hindering its polarization with consequent defective intracellular transfer and mitosis, inhibition of neutrophil chemotaxis, and reduced expression of adhesion molecules, and in addition, it has antioxidant and angiofibrotic properties, all of them might have contributed to the remission of proteinuria.

Prednisolone, cyclophosphamide, and azathioprine have been rarely used in cases with FMF-related glomerulonephritis,[3,12] but colchicine is the most common drug used to treat FMF-associated glomerulonephritis.[12] Said et al. documented important improvement in three patients with IgM nephropathy and FMF who took regular treatment with colchicine.[6] Cagdas et al. reported a case that was the remission of a patient with FMF and mesangial proliferative glomerulonephritis occurred after 3 years of colchicine treatment alone.[3] Colchicine treatment was successful for complete remission in our patient after 12 months of therapy.

All in all several kinds of glomerular diseases can be seen in FMF and FMF-associated glomerulonephritis may be more common than is now recognized. This is the first FMF case documented in which there may have been a correlation between resolution of a concurrent membranous glomerulonephritis and colchicine therapy, but further studies are necessary to evaluate between association of glomerulonephritis and FMF.

Declaration of interest: We declare that there is no conflict of interest or any financial support.

REFERENCES

[1] Jalkh N, Genin E, Chouery E, et al. Familial Mediterranean fever in Lebanon: Founder effects for different MEFV mutations. *Ann Hum Genet.* 2008;72:41–47.

[2] Topaloglu R, Ozaltin F, Yilmaz E, et al. E148Q is a disease-causing MEFV mutation: A phenotypic evaluation in patients with familial Mediterranean fever. *Ann Rheum Dis.* 2005; 64(5):750–752.

[3] Cagdas DN, Gucer S, Kale G, Duzova A, Ozen S. Familial Mediterranean fever and mesangial proliferative glomerulonephritis: Report of a case and review of the literature. *Pediatr Nephrol.* 2005;20(9):1352–1354.

[4] Yilmaz E, Ozen S, Balci B, et al. Mutation frequency of Familial Mediterranean fever and evidence for a high carrier rate in the Turkish population. *Eur J Hum Genet.* 2001;9(7):553–555.

[5] Fonnesu C, Cerquaglia C, Giovinale M, et al. Familial Mediterranean fever: A review for clinical management. *Joint Bone Spine.* 2008;15:1–7.

[6] Said R, Hamzeh Y. IgM nephropathy associated with FMF. *Clin Nephrol.* 1990;33:227–231.

[7] Said R, Nasrallah N, Hamzeh Y, Tarawneh M. IgA nephropathy in patients with FMF. *Am J Nephrol.* 1988; 8:417–420.

[8] Said R, Hamzeh Y, Tarawneh M. Rapid progressive glomerulonephritis in patients with FMF. *Am J Kidney Dis.* 1989;14: 412–416.

[9] Tekin M, Yalcinkaya F, Tumer N, Akar N, Misirlioglu M, Cakar N. Clinical, laboratory and molecular characteristics of children with familial Mediterranean fever-associated vasculitis. *Acta Pediatr.* 2000;89:177–182.

[10] Saatci U, Ozen S, Ozdemir S, et al. Familial Mediterranean fever in children: Report of a large series and discussion of the risk and prognostic factors of amyloidosis. *Eur J Pediatr.* 1997;156:619–623.

[11] Ozen S. Renal amyloidosis in familial Mediterranean fever. *Kidney Int.* 2004;65:1118–1127.

[12] Akpolat T, Akpolat I, Karagoz F, Yilmaz E, Kandemir B, Ozen S. Familial Mediterranean fever and glomerulonephritis and review of the literature. *Rheumatol Int.* 2004;24:43–45.