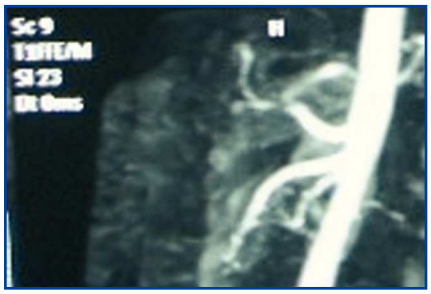

Figure 2. Oblique cut of angioresonance carried out six months after performing the first, with absence of stenosis in the renal artery.

Six months later the patient suffered a superficial phlebitis of the right lower extremity with deterioration in renal function (CrCl 86ml/min) and an increase in proteinuria, passing from 9 to 14.5g/24h. An angio-MRI was carried out which confirmed stenosis of the right renal artery, thus increasing the INR to >3. The stenosis was not evident in a follow-up x-ray (figure 2).

Since the proteinuria had not abated, in the context of myocarditis therapy was started with carvedilol and telmisartan, eicosapent, decreasing the proteinuria to 4.8g/24h with a CrCl of 75ml/min.

In 2006, given the new deterioration of renal function (CrCl 50ml/min), the possibility of immunosuppressant treatment was agreed with the patient and his family. Empirical treatment was begun with prednisone 0.5mg/kg/day and azathioprine 100mg/24h. The patient demonstrated a progressive decrease in proteinuria. Six months after beginning immunosuppressant treatment, proteinuria was 0.5g/24h with a CrCl of 80ml/min; thus the azathioprine was withdrawn, with just 10mg/24h steroids remaining.[4,5]

We reached a diagnosis of stage II CKD secondary to PAPS, associated with nephrotic-range proteinuria, corrected with azathioprine and steroids.

Discussion

Nephrotic syndrome is a rare finding that can be induced by thrombotic microangiopathy affecting the glomerular level. We could not discern the type of glomerular lesion since a renal biopsy was refused. However, given the gravity of the case and significant PAPS activity, we are inclined to determine focal segmental glomerulosclerosis in the context of a focal cortical atrophy, caused by probable renal infarctions. Furthermore, the patient presented with grade I obesity which, together with a decrease in renal mass, could bring about some degree of hyperfiltration.

1. Dayal NA, Isenberg DA. Endstage renal failure in primary antiphospholipid syndrome- case report and review of literature. Rheumatology 2003;42:1128-9.
2. Saracino A, Ramuni A, Pannarale G, et al. Kidney disease associated with primary antiphospholipid syndrome: clinical signs and histopathological features in an experience of five cases. Clinical Nephrol 2005;6:471-6.
3. Fakhouri F, Noel L, Suber J, et al. The expanding spectrum of renal disease associated with athiphospholipd syndrome. Am Jour Kid Dis 2003;46:1205-211.
4. Korkmaz C, Kabukcuoglu S, Isiksoy S, et al. Renal involvement in primary antiphospholipid syndrome and its response to immunosuppressive therapy. Lupus Journal 2003;12:760-5.
5. Dipankar B, Vatsala D, Amit K.D, et al. Steroid-responsive focal segmental glomerulosclerosis in primary antiphospholipid syndrome with successful pregnancy outcome. Nephrol Dial Trans 2005;20:1726-8.

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Renal amyloidosis in a female with familial Mediterranean fever: clinical response to treatment with colchicine and infliximab

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Dear Editor:

Familial Mediterranean fever (FMF) is an autoinflammatory, autosomal recessive inherited disorder, characterised by recurrent attacks of fever and serositis.[1] The identification of mutations in the MEFV gene has been of major assistance in early diagnosis in the majority of cases. Among the possible mutations, M694V is the most common, and is the mutation responsible for the most severe cases in heterozygous carriers.[2] The most significant long term complication is chronic renal failure caused by AA amyloidosis.[3] We describe the case of a female in which this disease presented itself in the form of nephrotic syndrome. Furthermore, we carry out a clinical follow-up of the response obtained after one year of combined colchicine and infliximab therapy.

Clinical case study

38 year old female, originally from Armenia, with no relevant personal history and a family history of father with nephropathy, who died at 50 years of age, and maternal aunt also with nephropathy. The patient was assessed for nephrotic syndrome in the nephrology department. In the assessment the patient described, in addition to oedemae in the lower extremities and palpebrae, non-specific lumbar pain. During the assessment for nephrotic syndrome, the patient required numerous admissions for hydropic decompensation.. A renal biopsy was carried out, with the discovery of eight glomeruli per section plane. These all showed a massive and diffuse deposit of congo red-positive amorphous, acellular and

eosinophilous matter (figure 1A). The immunohistochemical study showed congo red positivity for AA (figure 1B), this being the definitive diagnosis of amyloidosis AA. Given the family history of nephropathy, the patient's country of origin and the presence of secondary amyloidosis, a genetic study was carried out which showed the presence of M680I and M694V mutations in heterozygosis in the MEFV gene associated with FMF. Treatment with colchicine was started at a dose of 0.5mg every 8hrs/day and infliximab at a dose of 5mg/kg IV, in basal form, for two weeks, and thereafter every two months. The patient's subsequent progress after establishing the treatment regime is detailed in table 1.

Discussion

FMF manifests clinically in the form of attacks of fever, peritonitis, pleuritis or polyarthritis.[1] As a consequence of these inflammatory episodes, development of renal amyloidosis is common, worsening the prognosis.[3] Gingold-Belfer et al.[4] describe the case of a female patient in whom nephrotic syndrome was the primary manifestation of FMF, detected via the presence of an M694V mutation. Similarly, in our patient the diagnosis of FMF was also made via an assessment for nephrotic syndrome, since her symptoms did not relate to the classic symptoms of FMF and thus its presence was not suspected. In the case which we have described, our attention was drawn to the already advanced stage of the disease at diagnosis, with findings of severe nephrotic syndrome and AA amyloid deposits in the kidney. Furthermore, the presence of two mutations was detected, one of which (M694V) is the most common and that which is found in the most severe cases[2] such as ours.

With regard to treatment, colchicine is the drug typically used to treat this condition.[3] In cases of intolerance (diarrhoea) or inefficacy, other therapeutic options are considered.[5] TNF-alpha is a proinflammatory cytokine which can play a role in FMF as well as the development of secondary amyloidosis.[6] TNF inhibitors can therefore be of use in FMF.[7] This is reflected in some publications, where it is described how anti-TNF-alphas, including infliximab, reduce the frequency of FMF attacks and, therefore, bring about a recovery from proteinuria.[6,7] Considering that our patient did not tolerate antiproteinuric drugs (ACEI, ARA II), and given the severity of proteinuria and deterioration of renal function, as well as the biopsy findings which demonstrated amyloidosis, we decided to use a combined treatment of colchicine and infliximab to assess her progress. This combined therapy has achieved a subjective improvement in the patient (there has been no hydropic decompensation throughout the year, nor admission for any other motive), as well as a recovery of renal function and a stabilisation in the proteinuria with an increase of albumin in the plasma. It is possible that this only partial response which we have obtained with combined therapy could be due to the fact that the disease presented itself without the typical symptoms, and it was its first complication (renal amyloidosis) that allowed us to reach a diagnosis, indicating that the disease was already advanced at the time of diagnosis. However, it could also be due to the fact that the patient was a carrier of the M694V mutation, which is associated with the most severe cases.

With regard to the tolerance and safety of infliximab, we have detected no adverse effect with this medication or any infectious complications during the period of its administration, indicating a good level of tolerance. In conclusion, an unusual presentation of FMF could delay diagnosis and, therefore, worsen the prognosis in these patients. For those cases in which amyloidosis is the manner through which a diagnosis of FMF is reached, a combined therapy of colchicine and infliximab could be of use at least to achieve a stabilisation of the disease.

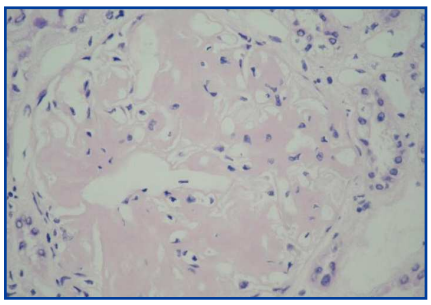

Figure 1a. Haematoxylin and eosin: glomerulus without cellular proliferation with coarse and diffuse deposits of eosinophilous and acellular matter, congo red positive.

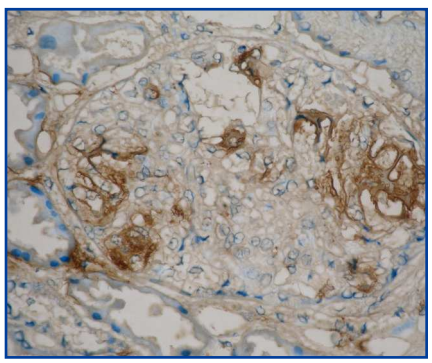

Figure 1b. Immunohistochemical test: positive stain for AA amyloid in the glomerulus.

1. Sohar E, Gafni J, Pras M, Heller H. Familial Mediterranean Fever. A survey of 470 cases and review of the literature. Am J Med 1967;43:227-53,
2. Sarkisian T, Ajrapetian H, Beglarian A, Shahsuvarian G, Egiazarian A. Familial Mediterranean Fever in Armenian population. Georgian Med News 2008;156:105-11.
3. Ben-Chetrir E, Levy M. Familial Mediterranean Fever. Lancet 1998;351: 659-64.
4. Gingold-Belfer R, Bergman M, Ori Y, Salman H. Nephrotic syndrome as a first manifestation of Familial Mediterranean Fever. Harefuah 2006;145:706-8.
5. Nakamura A, Matsuda M, Tazawa K, Shimojima Y, Ikeda S. Successful treatment with infliximab and low-dose methotrexate in a Japanese patient with Familial Mediterranean Fever. Intern Med (Tokio Japan) 2007;46:1247-9.
6. Metyas S, Arkfeld DG, Forrester DM,

Table 1. Development of the analytic parameters alongside combined therapy (colchicine+infliximab)

	Pre-treatment	Post-treatment				
	01/2008	02/2008	03/2008	08/2008	12/2008	02/2009
P Cr (mg/dL)	2	2.5	1,3	1.3	1.3	1.2
Chol (mg/dL)	369	378	432	342	246	295
TG (mg/dL)	455	421	352	238	210	224
Alb (g/dL)	1.9	1.6	1.7	2.5	2.6	2.9
CrC (ml/min)	19.7	16	21	19	45	31
Urine proteinuria 24h (g/24h)	17.22	12.50	12.47	7.35	10.7	7.10

P Cr: plasma creatinine; Chol: cholesterol; TG: triglycerides; Alb: albumin; CrC: creatinine clearance.

Ehresmann GR. Infliximab treatment of Familial Mediterranean Fever and its effect on secondary AA amyloidosis. J Clin Rheumatol 2004;10:134-7.

7. Ozgocmen S, Ozçakar L, Ardicoglu O, Kocakoc E, Kaya A, Kiris A. Familial Mediterranean Fever respond well to infliximab: single case experience. Clin Rheumatol 2006;25:83-7.

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Disease caused by anti-glomerular basement membrane antibodies and haematoma of the recti

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Dear Editor:

We present a case of disease caused by anti-GBM Ab which, on treatment with plasmapheresis, presented a massive haematoma of the recti, a serious complication not previously described.

The case concerns a 57 year old female who attended hospital with lumbar pain, haematuria, febricula and flu-like syndrome which had been developing for two weeks. Creatinine of 3.5mg/d was notable, with normal history and sediment with haematuria and proteinuria. Ultrasound normal. Urgent anti-GBM Ab positive in the capacity of 1200 UI/ml with negative ANCA. Renal biopsy showed crescentic glomerulonephritis caused by anti-GBM Ab, with 85% epithelial half-moons in the cellular phase.

Treatment with methylprednisolone, cyclophosphamide and plasmapheresis (anticoagulation with citrate and replacement initially with albumin and later combined with plasma). Deterioration of renal function persisted with creatinine of 8.4mg/dL and oliguria. Haemodialysis without heparin was begun. After thirteen days the patient complained of pain in the hypogastrium and left iliac fossa following a coughing episode. An abdominal mass and anaemia of four points were apparent. An abdominal CT revealed a haematoma of the left anterior rectus sheath (figure 1). Three concentrates were transfused. A coagulation test including factors was normal except for an Ivy value of ten minutes. Three days later there was new pain in the right iliac fossa, with paralytic ileus and anaemia of three points. A CT revealed a haematoma in both anterior rectus muscles which extended towards the Retzius space and pelvis (figure 2). It pinpointed four concentrations of erythrocytes. The departments of surgery and interventional radiology consulted, deciding on conservative expectant treatment and associating antibiotics (clavulanic amocycillin) as well as parenteral nutrition.

After one week the ileus was resolved, but the patient began to experience sudden dyspnoea with the normal prescription. A scintigraphy confirmed a multiple pulmonary embolism. Treatment with a heparin pump was started with close monitoring. The haematoma and pulmonary embolism were resolved without consequence but the patient continued to be dependent

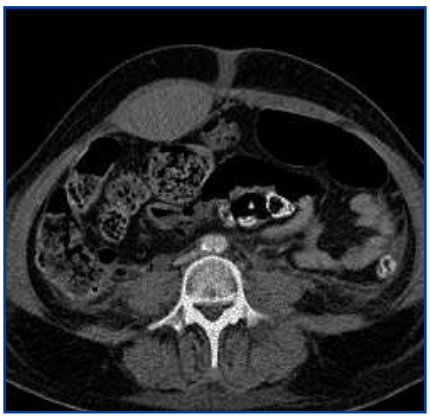

Figure 1. Abdominal CT: right rectus haematoma.