Journal of Nephrology & Therapeutics

Melfa and Scarpioni, J Nephrol Ther 2016, 6:4
DOI: 10.4172/2161-0959.1000256

Case Report Open Access

Renal Failure Due to MYH9-Related Disorder (Macro-Thrombocytopenia): Peritoneal Dialysis as a First Choice Therapy and Kidney Transplant from Living Donor

Luigi Melfa* **and Roberto Scarpioni**

Operative Unit Nephrology and Dialysis Piacenza, Piacenza Hospital, Piacenza, Italy

***Corresponding author:** Luigi Melfa, Operative Unit Nephrology and Dialysis Piacenza, Piacenza Hospital, Vias Taverna 49, Piacenza 29100, Italy, Tel: +393478543282; E-mail: L.MELFA@AUSL.PC.IT

Received date: August 03, 2016; **Accepted date:** August 18, 2016; **Published date:** August 25, 2016

Introduction

MYH9-related disorders, previously distinguished in four syndromes (Epstein syndrome, Fechter syndrome, Sebastian syndrome, May-Hegglin anomaly) based on the combination of different clinical findings at the time of diagnosis; appear to be only one rare nosological entity (MYH9RD). It has been recognized that they are all phenotypic variants due to mutation in MYH9 gene (heterozygous pathogenic variants) and that the clinical findings often worsen throughout life as a result of late onset of non-hematologic manifestations [1].

Epidemiology

MYH9RD is a very rare disease. The Italian Registry includes 180 affected individuals. The prevalence of the disorder in Italy is 3:1,000,000.

In all individuals macrothrombocytopenia is present at birth. Mean platelet diameter is 4.5 mcm (C.I. 95% 4.2-4.8) [2]. Thrombocytopenia ranges from mild to severe.

Presence and severity of spontaneous bleeding tendency correlate with the degree of thrombocytopenia, but most affected individuals have no spontaneous bleeding [3]. Life-threatening bleeding is rare.

The non-congenital manifestations of MYH9RD can develop anytime between infancy and adulthood.

The overall annual rates per 100 affected persons are 1.71 for sensorineural hearing loss, 0.77 for nephropathy, and 0.57 for cataract [3].

Glomerular nephropathy arises with proteinuria and microhematuria. The mean age at onset is 27 [3].

Out of those who develop renal disease, 72 percent are diagnosed before the age of 35. In most affected individuals with nephropathy, kidney damage is progressive and evolves to renal disease (ESRD). Among those with nephropathy, the overall annual rate for 100 affected people for progression to ESRD is 6.79 [3].

Case Report

We report the case of a young woman, a 30-year-old only daughter woman suffering from severe thrombocytopenia due to MYH9RD who reached ESRD, started peritoneal dialysis and after that was successfully renal transplanted from living donor.

At the age of 4 the first response of thrombocytopenia (PLT 84.000/mm^3) was diagnosed, the platelet function test within normal limits. However, the exam of cytoskeleton organization showed study-worth alterations. In the subsequent years, platelet count showed values between 6.000/mm^3 and 30.000/mm^3. Moreover, hemorrhagic manifestations were not related (epistaxis, menomethrorragia, bleeding gums, anemia or petechiae) (Figure 1).

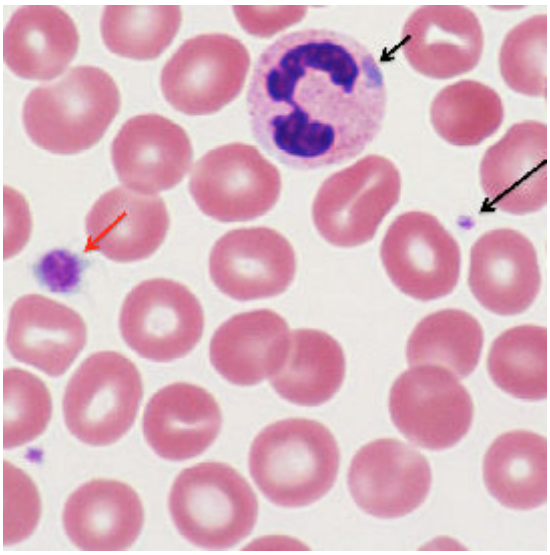

Figure 1: MYH9-related disorder with characteristic inclusion bodies in the neutrophils (small black arrow) and large platelets (red arrow). Normal- sized platelets are also seen (long black arrow).

At the age of 17 "May-Hegglin anomaly" was diagnosed by molecular genetic testing. The anomaly was attributable to the R702 mutation occurred in MYH9 gene, which encodes the non-muscle myosin heavy chain IIA (NMMHCIIA). It was a "*de novo*" pathogenetic variant; indeed, it wasn't documented in the patient's parents (as occured in almost 20-30 percent of cases). Urinalysis showed proteinuria. Renal biopsy was not performed, because it was contraindicated by the bleeding risk linked to low platelet count and by the advanced stage of renal insufficiency.

At the age of 27 kidney function worsened (serum creatinine up to 3 mg/dl), associated with blood hypertension. Because of the gradual progressive worsening of renal function (serum creatinine up to 7 mg/dl) two years later patient started peritoneal dialysis, via a surgical Tenchkoff catheter placement, preceded by platelet concentrates

infusion. Peritoneal dialysis treatment was chosen in order to provide home care dialysis and promote employment, but above all to reduce the risk of bleeding, related to the use of heparin in hemodialysis.

After one year's dialysis, living donor kidney transplantation was performed by receiving a kidney from her mother. On postoperative day 1, her platelet count decreased from (35000/mmc) to 24000/mmc without intraoperative transfusions. Surgical findings revealed no specific problems and the kidney were perfused homogeneously. In the same operating session, the peritoneal catheter was also removed. Unfortunately, three days after the intervention, due to diffuse bleeding of the abdominal wall, a new surgical intervention to remove hematoma compressing the kidney was necessary, with accurate abdominal wall hemostasis.

During the surgery, four packed red blood cells units and two packed of platelet were necessary because of acute anemia a thrombocytopenia (Hb 8.2 g/dl from 10.2 g/dl; PLT 20000/mmc).

Immunosuppressive drug regimen included basiliximab as induction and tacrolimus and steroids as maintaining therapy. The patient showed quick diuresis recovery, improving renal function (serum creatinine=1.2 mg/dl on postoperative day 5): 20 days later the patient was discharged in good clinical condition. Her cell count showed:

PLT=47.000/mm3, Hemoglobin=10 g/dl, Hematocrit=30.4%, serum creatinine levels=1.2 mg/dl (GFR=61 ml/min calculated by CKD-EPI)

After six months PLT count is 31000/mmc; serum creatinine is 1,5 mg/dl; the patient is doing well.

Pathogenesis

The histological renal damage in MYH9RD is not fully understood yet. NMMHCIIA protein is strongly expressed in podocytes and mesangial cells [4]. The protein distribution is reported to be altered in MYHRD [4]. Defective NMMHCIIA protein, as major component of the actin myosin contractile apparatus in the podocyte foot process, could damage the glomerular filtration barrier by altering the podocyte cytoskeleton [5].

As shown by Pecci et al. [6] in a genotype-phenotype correlation study of 108 patients with MYH9RD, all the subjects with mutations in the motor domain of the protein reported severe thrombocytopenia and developed glomerulopathy before the age of 40. On the other hand, those with mutations in the tail domain had a much lower risk of glomerulopathy and significantly higher platelet counts. Furthermore, a mutation at residue 702 (as occurred in our patient) was reported to be associated with severe thrombocytopenia and glomerulopathy at a juvenile age.

Histology

The renal pathological data of MYH9RD has been rarely reported, because the biopsy is contraindicated by the high bleeding risk. The few available reports [4,7] suggest that the pathological feature underlying progressive nephritis could be focal segmental glomerulosclerosis (FSGS) preceded by a mild mesangial proliferation and expansion, with focal GBM thickening.

Kidney abnormalities are seen in about 30-70 percent among MYH9RD patients. Patients may show microscopic hematuria, with or without proteinuria. Proteinuria may remain in sub-nephritic range or may become nephritic [8]. The combination of glomerulopathy, sensorineural deafness and, in some cases, cataracts may mimic Alport syndrome, but the other features (particularly abnormal platelets and autosomal dominant mode of inheritance) should aid in the clinical distinction.

Conclusion

In May-Hegglin anomaly bleeding risk is generally mild, but not negligible [9] and this is to be kept in mind, as described herein. Spontaneous bleeding or postpartum life threatening have rarely been reported [10]. In case of transplantation or surgery, the manual counting of platelets is recommended, as automatic can underestimate the number, because of the typical presence of giant platelets. A specific treatment doesn't exist. At any surgeries the use of desmopressin, the antidiuretic analog, with mild hypertension activity, has been proposed [11,12]. However, in our patient, desmopressin infusions test (Minirin 0.4 mcg/kg), performed some years before, did not induce any improvement in primary haemostasis.

A genetic diagnosis is mandatory for a correct prognosis of non-hematologic complications, kidney failure, in particular, for the treatment or prophylaxis.

In conclusion, as to our knowledge, our case highlights the renal risk in such a disease and it is another case of living kidney transplant performed in a patient with MYH9RD that can be added to very small case series in the literature [13,14].

References

1. Althaus K, Greinacher A (2009) MYH9-related platelet disorders. Semin Thromb Hemost 35: 189-203.
2. Noris P, Biino G, Pecci A, Civaschi E, Savoia A, et al. (2014) Platelet diameters in inherited thrombocytopenias: analysis of 376 patients with all known disorders. Blood 124: e4-4e10.
3. Pecci A, Klersy C, Gresele P, Lee KJD, Bozzi V, et al. (2014) MYH9-related disease: a novel prognostic model to predict the clinical evolution of the disease based on genotype-phenotype correlations. Hum Mutat 35:236-247.
4. Sekine T, Konno M, Sasaki S, Moritani S, Miura T, et al. (2010) Patients with Epstein-Fechtner syndromes owing to MYH9 R702 mutations develop progressive proteinuric renal disease. Kidney Int 78: 207-214.
5. Ghiggeri GM, Caridi G, Magrini U, Sessa A, Savoia A, et al. (2003) Genetics, clinical and pathological features of glomerulonephritis associated with mutations of nonmuscle myosin IIA (Fechtner syndrome). Am J Kidney Dis 41: 95-104.
6. Pecci A, Panza E, Pujol-Moix N, Klersy C, Di Bari F, et al. (2008) Position of nonmuscle myosin heavy chain IIA (NMMHC-IIA) mutations predicts the natural history of MYH9-related disease. Hum Mutat 29: 409-417.
7. Han KH, Lee H, Kang HG, Moon KC, Lee JH, et al. (2011) Renal manifestations of patients with MYH9-related disorders. Pediatr Nephrol 26: 549-555.
8. Singh N, Nainani N, Arora P, Venuto RC (2009) CKD in MYH9-related disorders. Am J Kidney Dis 54: 732-740.
9. Balduini CL, Pecci A, Savoia A (2011) Recent advances in the understanding and management of MYH9-related inherited thrombocytopenias. Br J Haematol 154: 161-174.
10. Pecci A, Gresele P, Klersy C, Savoia A, Noris P, et al. (2010) Eltrombopag for the treatment of the inherited thrombocytopenia deriving from MYH9 mutations. Blood 116: 5832-5837.
11. Mannucci PM, Remuzzi G, Pusineri F, Lombardi R, Valsecchi C, et al. (1983) Deamino-8-D-arginine vasopressin shortens the bleeding time in uremia. N Engl J Med 308: 8-12.
12. Mannucci PM (1998) Hemostatic drugs. N Engl J Med 339: 245-253.

13. Fabbian F, Ricci F, De Giorgi A, Forcellini S, Scanelli G (2010) The May-Hegglin anomaly in a kidney transplant recipient. NDT Plus 3: 312.
14. Min SY, Ahn HJ, Park WS, Kim JW (2014) Successful renal transplantation in MYH9-related disorder with severe macrothrombocytopenia: First report in Korea. Transplant Pro 46: 654-656.