Successful Kidney Transplantation in *MYH-9*-Related Disease Presenting with Severe Macrothrombocytopenia

Ciddi Makrotrombositopeni ile Prezente Olan *MYH-9* İlişkili Hastalıkta Başarılı Böbrek Nakli

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To the Editor,

MYH-9-related diseases are a group of genetic diseases caused by mutations in the *MYH-9* gene, which encodes for the non-muscle myosin heavy chain IIA (NMMHC-IIA), showing autosomal dominant inheritance. NMMHC-IIA protein is found in platelet, granulocyte, podocyte, mesangial, tubule epithelial, and cochlear cells and, when they are mutated, symptoms may occur due to loss of functions of these cells [1,2]. Although renal failure, hearing loss, and cataracts can be seen with some subtypes, macrothrombocytopenia is seen in almost all groups of *MYH-9*-related diseases [3]. Here, we present the case of a successful kidney transplantation for a patient who presented to our hospital with the diagnosis of immune thrombocytopenic purpura (ITP) and chronic kidney disease and was found to have *MYH-9*-related disease in examinations for macrothrombocytopenia.

A 24-year-old male, diagnosed with ITP at the age of 4 years, applied for kidney transplantation while receiving hemodialysis treatment for chronic kidney failure for 2 years. The platelet levels of the patient, who was unresponsive to steroid, IVIG, rituximab, and eltrombopag treatments for ITP, ranged between $5x10^3$/μL and $15x10^3$/μL. There was no proteinuria or hematuria in the urine sample and no family history of renal failure. Macrothrombocytopenia and schistocytes were observed in the peripheral smear. Coagulation and hemolysis test results were normal. The bone marrow biopsy was consistent with normocellular bone marrow showing moderate hyperplasia in the megakaryocytic series. Bernard-Soulier syndrome was excluded by flow cytometric analysis of the normal expression of CD42 (Gp1b) and von Willebrand factor (VWF) type 2B was ruled out by normal VWF Ag levels. Platelet aggregation was abnormal based on PFA 200 (collagen/epinephrine and collagen/ADP). The ANA panel, ds-DNA, c-ANCA, p-ANCA, anti-PR3, anti-MPO, β2 glycoprotein 1 immunglobulin (Ig)M, IgG, anticardiolipin IgM, and IgG antibodies were all negative. ADAMTS-13 antigen and activity levels studied for the differential diagnosis of microangiopathic hemolytic anemia (TTP/AHUS) were found to be normal. The patient was also evaluated in terms of *MYH-9*-related diseases. Hearing loss and cataract findings were not detected in an examination performed by a consultant. Whole-exome and copy number variation (CNV) analysis was requested to clarify the possible genetic etiopathogenesis. With those results, eculizumab treatment (4 doses) was applied considering that the patient might have AHUS, but no increase in platelet levels was observed. Deciding to proceed to transplantation with blood transfusion, on the day of the operation, the platelet level was increased with platelet transfusions (10^2x10^3/μL) and living-donor kidney transplantation was performed without any complications after a programmed procedure. Platelet transfusion efficiency was also tested by rotational thromboelastography (ROTEM) for this patient, who was given transfusion support with a platelet value >$50x10^3$/μL after the transplantation for 10 days. The platelet level started to drop again after 10 days; however, no bleeding complications were seen during follow-up. His serum creatinine level had increased to 11.3 mg/dL (glomerular filtration rate: 10 mL/min/1.73 m^2) but he was discharged with a creatinine level of 1.6 mg/dL after transplantation and prescribed mycophenolate mofetil, prednisolone, and tacrolimus. A previously reported pathogenic heterozygous c.287C>T (p.Ser96Leu) change in the *MYH-9* gene was detected in whole-exome and CNV analysis during follow-up [4]. The heterozygous nature of this change was found to be compatible with the autosomal dominant inheritance pattern of the *MYH-9*-related phenotype. With this result, the patient, who was diagnosed with *MYH-9*-related disease, is still being followed without any problems for approximately 2 years at the time of writing.

In conclusion, young patients with renal failure, hearing loss, visual defects, and/or thrombocytopenia should be evaluated in terms of *MYH-9*-related diseases and genetic analysis should be performed to guide the diagnosis and prognosis. Kidney transplantation is a valuable option in cases of chronic renal failure in *MYH-9*-related disease [5,6,7]. Multidisciplinary approaches and transfusion protocols guided by viscoelastic tests will increase the success of kidney transplantation in these patients.

Keywords: *MYH-9*-related disease, Macrothrombocytopenia, Kidney transplantation

Anahtar Sözcükler: *MYH-9* ilişkili hastalık, Makrotrombositopeni, Böbrek nakli

Ethics

Informed Consent: Written informed consent was obtained from the patient.

Authorship Contributions

Concept- M.C.B, O.M.A.; Design- M.C.B, O.M.A.; Data Collection or Processing- M.C.B.; Analysis or Interpretation- M.C.B, O.M.A.; Literature Search- M.C.B, O.M.A.; Writing- M.C.B, O.M.A.

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