LETTERS

Membranous glomerulopathy secondary to chronic myeloid leukemia

Dear Editor,

Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm resulting from Philadelphia (Ph) chromosome translocation[1]. Immunoglobulin (Ig) A nephropathy, focal segmental glomerulosclerosis, thrombotic microangiopathy, and membranous glomerulonephritis (MG) have been detected in kidney biopsies of some CML patients[2]. However, the presence of MG as a paraneoplastic renal manifestation is infrequent, with only two cases reported to date[3].

A 33-year-old man presented to our department with fatigue, nausea, and splenomegaly without hypertension and thromboembolic events. Leukocytosis, thrombocytosis, hypoalbuminemia, decreased glomerular filtration rate, proteinuria, albuminuria, hypercholesterolemia, mildly increased D-dimer level, normal complement component 4 level, and mildly decreased complement component 3 level without auto-antibodies were detected. Hypercellularity, myeloid hyperplasia, erythroid and lymphoid cell suppression, and dysmegakaryopoiesis were detected via bone marrow evaluation. The polymerase chain reaction performed- using bone marrow cells revealed a BCR-ABL fusion transcript (40 %). The breakpoint cluster region was major. Consequently, the patient was diagnosed with the accelerated phase Ph+ CML. Renal biopsy revealed diffuse basal membrane thickening, mesangial matrix expansion, a mild proliferation of mesangial cells, and interstitial fibrosis (15-20 %) with mild Ig G deposition without crescent formation, necrosis, tumor cell infiltration (plasma and leukemia cells), or lambda or kappa deposition. MG secondary to the paraneoplastic effect of CML was diagnosed, and treatment for the underlying disease (CML) and methylprednisolone were administered. Imatinib, tenofovir alafenamide, atorvastatin, and methylprednisolone were administered orally. Owing to pulmonary aspergillosis development, methylprednisolone treatment was gradually tapered and stopped. No heparin or antiplatelet drugs were administered to prevent the thromboembolic complications of the nephrotic syndrome because thrombocytopenia was detected secondary to imatinib treatment. As BCR-ABL1 transcript levels still exceeded the target levels [<10 % after three, <1 % after six, and <0.1 % after 12 months of therapy with tyrosine kinase inhibitors (TKI)], imatinib (400 mg/day), dasatinib (100 mg/day), and bosutinib (500 mg/day) were administered consecutively until adequate molecular response (MR) was achieved. Partial MR (1.64 %) was attained after three months of bosutinib treatment. Proteinuria improved accordingly with MR to CML treatment. At the last control, proteinuria decreased to 10 g/day. The patient felt better and was scheduled for bone marrow transplantation because of the lack of substantial MR of BCL-ABL1 transcript levels, which should be <1 % after 12 months of treatment with alternative tyrosine kinase inhibitors (resistance to TKI).

Identifying secondary diseases that could lead to glomerulonephritis is essential while evaluating patients with nephrotic syndrome. In the present case, the nephrotic syndrome was caused by membranous glomerulopathy based on renal biopsy, and membranous glomerulopathy was secondary to hematological malignancy based on the absence of anti-PLA2R. The proteinuria response correlated with the MR to TKI-treated CML monitored via BCR-ABL1 transcript levels. The presence of leukocytosis and splenomegaly provided important clues for the paraneoplastic association of MG. The literature suggests that the majority of CML patients develop MG (10/13 cases) after stem cell transplantation complicated with graft-versus-host disease (GVHD) due to GVHD-related glomerulopathy mediated by immune complexes. In contrast, cases without GVHD are caused by immune reactions triggered by intraglomerular chimeric cells. MG was reported in a case due to immune-mediated complication of interferons formerly used for CML treatment. Only two patients have been reported to present with MG, nine months and four years after CML diagnosis[3]. To our knowledge, the reported patient represents the third reported case of paraneoplastic presentation of MG secondary to CML.

Keywords: Glomerulonephritis, membranous; leukemia, myeloid; leukocytosis

Conflicts of interests
Authors declare no conflicts of interest.

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