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LETTER TO THE EDITOR

Reply to the letter of Dr Merdin

Dr Merdin kindly makes suggestions about the design of our study and asks for more information about the infectious and immunosuppressive history of our monoclonal B-cell lymphocytosis (MBL) patients with monoclonal B-cell lymphocytosis (MBL).

In our study, we incidentally found the coexistence of five cases of MBL and monoclonal gammopathy of undetermined significance (MGUS) in a cohort of kidney transplant recipients at a median of 15 years after transplantation.[1] MBL and MGUS are two pre-malignant lymphoproliferative disorders of terminally differentiated B cells. Clinically, MBL and MGUS share common features, such as an indolent course, a late-onset age distribution, a low rate of progression and an increased susceptibility to infections. MBL and MGUS are also the precursor states of two hematologic malignancies: chronic lymphocytic leukemia (CLL) and multiple myeloma (MM), respectively.

Merdin et al[2] recently described the clinical presentation of a patient who had both CLL and MM.[3,4] Despite the simultaneous occurrence of CLL and MM is extremely rare and has been reported only anecdotally, Rawluk et al[3] suggest that the association between these malignancies might be detected more frequently than it was previously if careful monitoring is routinely performed in these subjects.

It is unknown whether the coexistence of disorders developing from plasma cells (MGUS and MM) and B cells (MBL and CLL) is a mere coincidence or whether it is the expression of an altered signaling pathway of a common B-cell progenitor. The best way to investigate their possible clonal relationship is to perform cytogenetic and genomic analyses of the proliferating B cells. Unfortunately, we did not perform the aforementioned analyses in our patients, thus, future studies are necessary to expand knowledge in this field.

The immunosuppressive therapy of the five patients is clearly reported in our study. Induction therapy with basiliximab was performed in only one patient. All the patients were on calcineurin inhibitor (CnI)-based immunosuppression in combination with steroids at the diagnosis of MBL; only two patients received triple therapy (CnI, mycophenolate mofetil, and steroids). The median cyclosporine trough level was in range with the transplant vintage, and no adjunctive therapies for treating rejections were used. In our patients, over-immunosuppression to preserve graft function was avoided, even though we are concerned about the cumulative effect of the prolonged immunosuppressive therapy (more than 15 years) to which the patients were exposed. To date, there is no clear evidence that immunosuppression can elicit the development of MGUS or MBL,[5] but we cannot exclude the possibility that long-term immunosuppression can promote a state of cellular senescence favoring the proliferation of mature B cells.

Regarding the risk of infection, we reported only one case of severe bacterial infection that required hospitalization. The viral replication of cytomegalovirus and Epstein-Barr virus was clinically asymptomatic and without sequelae. A further case of severe infection (bacterial sinusitis), successfully treated with antibiotics, occurred in a male patient after the publication of the article. These few episodes, which are partly favored by chronic immunosuppression, do not allow the generalization of our data on the risk of infection in patients with MBL.

CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

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