eosinophils and GVHD, it is therefore important to have a validation of similar results by 2 independent teams on 2 different organs in patients with GVHD.

The fact that eosinophils show signs of activation both in blood[3] and target organs[2,4] of patients with acute flares of GVHD raises the question of their deleterious effect on target organs in GVHD. Signs of eosinophil activation, both in blood and target organs, were also found in patients with severe eosinophilic syndromes.[5] Experimental studies to assess the role of eosinophils in target organ damage cannot be performed in humans for ethical reasons. However, there is an increasing amount of clinicopathologic data that links eosinophils to severity of target organ damage. To remain in the field of GVHD, eosinophils are linked to severe forms of GVHD when detected in bone marrow, gut, and conjunctiva, but they are also associated with a striking resistance to conventional therapy in fasciitis. This rare form of GVHD[6] shares many clinicopathologic features with eosinophilic fasciitis[7] except for the dramatic response to steroid therapy.

Therefore, systematic study of eosinophils in biopsies of patients with GVHD could contribute to assess GVHD severity and thus may help to modulate immunosuppression therapy.

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To the editor:

Heterozygous PU.1 mutations are associated with acute myeloid leukemia

We appreciate the information from Lamandin et al,[1] in which his group was unable to identify PU.1 mutations in their patient samples with acute myeloid leukemia (AML). As a result, we have reviewed all of our own primary sequencing data and confirmed the results that were reported in our article.[2] As reported in the article, sequencing results from samples containing mutations were independently repeated 3 to 6 times, including repetitions of the polymerase chain reaction (PCR) and sequencing with alternative primers. In 3 patients we had available both cDNA and genomic DNA at diagnosis, and the mutation was detectable from both sources. Since the publication, we have detected an additional PU.1 mutation in a patient with t(8;21) AML. We agree that our use of screening by direct DNA sequencing of both cDNA and genomic samples, as well as ethnic differences in the patient populations, could account for some of the differences between our results.

We respectfully believe that PU.1 mutations do occur in some patients with primary AML, as has been found with another myeloid transcription factor, C/EBP alpha.[3-5] Additional studies analyzing larger numbers of patients from different ethnic groups may be needed to assess the true frequency of such mutations. At the same time, as has been described in the case of C/EBP alpha, other mechanisms affecting PU.1, such as down-regulation[6] and/or inhibition of activity,[7,8] may also implicate loss of PU.1 function in other cases of AML that do not harbor mutations.

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