to directly deplete CD4+ T cells, and the mechanism of rituximab-induced immunosuppression is much more likely to be via suppression of humoral immunity, which may take many months to normalize after exposure.4

In pointing out our error, it does highlight the importance of the interplay between these 2 arms of the immune system, and also the effect of combining therapies that may influence both B- and T-cell immunity. Indeed, there are recent worrying reports of infections occurring after rituximab administration that are more typically associated with T-cell immunosuppression. Most striking are those of JC papovavirus–related progressive multifocal leukoencephalopathy and cytomegalovirus infection in patients who received periautotransplantation rituximab. Moreover, these patients had an unusually prolonged depression of CD4+ cell counts.5 Delayed CD4+ cell reconstitution has been reported by others in patients receiving rituximab after autologous transplantation.6 Although there may be other reasons contributing to alterations in T-cell immunity in these reports, they highlight that one should not currently dismiss rituximab’s potential influence, either quantitatively or qualitatively, on T-cell immunity. Unfortunately, many of the described cases of opportunistic infections in patients treated with rituximab do not report T-cell subsets. Indeed, with the increasing use of rituximab, in particular in combination with therapies that are known to alter T-cell immunity, physicians should carefully consider rituximab’s potential immunosuppressive effects. Furthermore, in an attempt to clarify the impact of rituximab on T-cell immunity, further studies quantitating T cells are warranted.

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References

To the editor:

Allogenic bone marrow transplantation: not a treatment yet for familial Mediterranean fever

We recently heard about the case of an 8-year-old Arabic patient who, following the recent article by Milledge et al,1 was offered a bone marrow transplantation (BMT) by a private institution to cure his familial Mediterranean fever (FMF). This boy has a very good general constitution but is still suffering from recurrent bouts of fever with abdominal pain, although he has been on colchicine 3 × 0.5 mg a day for 2 years. No alternative drug has been tried. This little boy has no evidence of amyloidosis. While, in this patient, 2 Met694Val mutations were identified in MEFV, the gene responsible for FMF, no MEFV screening was performed in his HLA-identical younger brother, the designated matched family donor.

We would like to stress the fact that BMT is a life-threatening and expensive procedure that has not proved to be a cure for FMF at this point. We recommend that the following issues be addressed in the rare FMF patients resistant to colchicine: (1) Does the patient indeed suffer from FMF? The diagnosis should be confirmed by a well-experienced clinician and/or by genetic testing. (2) Does he/she really take appropriate doses of colchicine? Is there any possibility of defective absorption of colchicine, allergy, or intolerance to colchicine? (3) Have all medical approaches been exhausted? If the patient truly does not respond to a maximal tolerated dose of colchicine (up to 2-2.5 mg a day, dose split up throughout the day), and if compliance is not involved, other treatments should be discussed, such as interferon α,2 and possibly thalidomide3 or anticytokines. (4) In any case, colchicine treatment should not be stopped because of the risk of developing amyloidosis.

Even when the patient is refractory to medical treatment and suffers from intractable and debilitating FMF, it is still debatable whether and when BMT should be considered. We agree that this treatment might possibly improve FMF symptoms, since this disease may be regarded as a hematopoietic disorder and BMT has sometimes shown to work in preliminary trials in other inflammatory disorders, such as rheumatoid arthritis. However, given the morbidity and mortality associated with BMT, and given that FMF is a self-limited disease with an overall good prognosis when colchicine is properly adjusted, we maintain that BMT has no role in the current treatment of FMF in the general medical community and should be contemplated only in the setting of a carefully conducted research protocol, if at all. Moreover, the ethical issue of offering this high-risk, unproven procedure to children is particularly troubling, even in the setting of a well-designed study.

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