To the Editor:

Dr Wright et al describe a subset of patients with common variable immunodeficiency characterized by the immunophenotypic finding of an expansion of CD8+ lymphocytes coexpressing CD57 and HLA-DR. They noted an increased incidence of anergy in these patients. As the authors mentioned, an increase in cells of this phenotype is characteristic of patients with early human immunodeficiency virus (HIV) infection. They did not mention that it is also associated with infection by or exposure to other viruses, especially cytomegalovirus, in healthy blood donors as well as in immunosuppressed individuals. The authors did not say whether they investigated the possibility of viral infection in their patients. It is possible that the subset of patients that they have identified is one with more advanced or more severely impaired cellular immunity, and that the immunophenotypic findings are secondary to opportunistic viral infection. A less likely explanation would be that this subset of patients is one with chronic exposure to blood products or other sources of cytomegalovirus antigen. The authors state that the phenotypic changes were stable over 2 to 7 months. Additional follow-up information about both subsets of patients might be useful. It would be of interest to determine whether patients with normal phenotype progressed to an abnormal phenotype over time, and whether patients with abnormal phenotype developed evidence of cytomegalovirus or other opportunistic viral infection.

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REFERENCES


RESPONSE

To the Editor:

We thank Dr Dow for her comments regarding our manuscript. We considered the possibility that chronic viral infection may have contributed to the phenotypic changes noted in our common variable immunodeficiency (CVID) patients, as suggested by Dr Dow. Published accounts report a moderate degree of CD8/CD57 lymphocytosis in normal (asymptomatic) individuals with serologic evidence of previous exposure to cytomegalovirus (CMV). However, serologic documentation of previous or current CMV infection is not possible in these agammaglobulinemic patients due to their deficient humoral immune response; furthermore, the overwhelming majority are receiving replacement therapy with immune globulin that is CMV antibody-positive. There was no clinical evidence of CMV infection in our CVID groups with or without phenotypic changes. None of the patients were systematically studied for evidence of CMV shedding; however, there also is no indication that viral cultures were used as a criteria for determining infection status in the studies cited by Dr Dow.

Further comparison of the immunophenotype of our CVID patient group and CMV antibody-positive individuals identifies a distinctive feature. A phenotypic change noted in the CVID patient subset was an elevated number and percent of HLA-DR+CD8 T cells, which was not observed in the CMV-seropositive normal individuals.

There is no obvious relationship between the immunopheno-

typic changes and exposure to blood products in that the majority of both patient groups had only received immune globulin (and no other blood products). Furthermore, the clinical data regarding these patients does not suggest that CD8/CD57 lymphocytosis develops as part of the progression of CVID because it is not found primarily in patients with a long-standing diagnosis of agammaglobulinemia. Rather, newly diagnosed patients as well as individuals with a long history of CVID fell into both immunophenotypic categories.

The wide spectrum of unrelated diseases associated with CD8/CD57 lymphocytosis suggests that both viral and nonviral antigenic stimuli can induce expansion of this T-cell subpopulation. CVID is a heterogeneous disorder in which it is still unclear whether the immunophenotypic changes we have described are a result of the basic immune defect underlying CVID or a consequence of chronic antigenic stimulation in these immunodeficient patients.

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CD8/CD57 lymphocytosis in common variable immunodeficiency [letter; comment]

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