NATURAL KILLER CELL NUMBERS AND ACTIVITY IN PATIENTS WITH CHRONIC AUTOIMMUNE THROMBOCYTOPENIC PURPURA

To the Editor:

Natural killer (NK) cells have the spontaneous ability to bind to and lyse malignant and nonmalignant cell targets. They are thought to be important not only in immunosurveillance but also in the regulation of hematopoiesis and B-cell development. Depressed numbers of NK cells and decreased NK activity have been reported in many malignant and nonmalignant chronic disease states, including autoimmune states and immune cytopenias. A number of reports have, on the other hand, described reduced NK activity in the presence of normal numbers of NK cells. Although the significance of suppressed NK cell activity in autoimmune pathogenesis is as yet unknown, NK cells appear to be capable of regulating B-cell immunoglobulin production and their defective activity in autoimmune diseases may have an influence on autoantibody production.

We have read with interest the recent report of Garcia-Suarez et al demonstrating increased numbers of CD3-CD56+ NK cells in patients with chronic autoimmune thrombocytopenic purpura (ATP) undergoing therapy. There have been several phenotypic characterizations of peripheral blood mononuclear cells in ATP, but it is well recognized that the determined number of cells of a subset does not necessarily reflect the functional status of the particular cell populations. Studies by our group and others have previously shown that patients with chronic ATP, and those with secondary ATP, have functionally suppressed NK cell activity (as measured by lysis of 51Cr-labeled K562 target cells), despite normal percentages and absolute numbers of NK cells.

Garcia-Suarez et al suggested that their results conflicted with our previous report and that this was because of the low number of patients studied by us (patients with chronic ATP n = 7; patients with secondary ATP n = 6), and the apparent mild degree of thrombocytopenia in our patients (platelet count range 2 to 110 x 10^9/L, mean 59 ± 37). We would suggest that the results of Garcia-Suarez et al in fact support and extend our original findings. The patients studied by us were newly diagnosed with chronic ATP, and only 4 with idiopathic chronic ATP and 5 with secondary ATP had received therapy at the time of study. The 10 nontreated stable patients that Garcia-Suarez studied (presumably similar to ours) had normal numbers of NK cell percentages, which corresponds to our observations. Furthermore, we reported that there was a direct correlation between the duration of therapy and NK activity in our chronic ATP patient group; the increase in CD3-CD56+ NK cells in the therapy-dependent population reported by Garcia-Suarez et al correlates with this increased NK activity with therapy.

Taken together, the results suggest that suppressed NK activity in chronic ATP may be rescued by therapy and this may have an influence on autoantibody production.

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We have read with interest the comments of Semple and Freedman related to our recent report about the natural killer (NK) cells in chronic autoimmune thrombocytopenic purpura (ATP) patients.\(^1\) NK cells represent a subset of lymphocytes with heterogeneous expression of cluster differentiation (CD) antigens.\(^2\) The different groups of NK cells, defined according to the expression of CD antigens mainly used as “markers” of these lymphocytes (CD56, CD16, CD57, and CD11b), show different levels of spontaneous cytotoxic activity.\(^2\)\(^3\)

The nonassociation between the number of NK cells in peripheral blood mononuclear cells (PBMCs) and their cytotoxic activity has been shown in malignant and nonmalignant diseases.\(^4\)\(^5\) This discordance may be explained by a redistribution of the NK cells subset in peripheral blood from the studied patients and/or for an intrinsic abnormality of the NK cells cytotoxic function.

We have found in the analyzed chronic ATP patient population (23 with severe chronic ATP and 10 with stable disease) that the CD56\(^{+}\)CD3\(^{-}\) NK cell expansion is associated with the severity of the disease.\(^1\) Semple and Freedman reported a normal percentage of NK cells in a population of 17 ATP patients, but only 5 of these patients had severe disease.\(^6\) The investigators also stated that there was a direct correlation between the duration of therapy and NK activity in the ATP patient group. The ATP patients treated in the Semple and Freedman study had received steroids for 1 day (2 cases), 2 days (1 case), and 28 days (1 case). In our chronic severe ATP patient group, we do not consider that the expansion of CD56\(^{+}\)CD3\(^{-}\) NK cells is related to the duration of therapy. We have found that the increased percentage of CD56\(^{+}\)CD3\(^{-}\) NK cells in patients with severe ATP is previous to the commencement of treatment, and it is mainly observed in patients whose disease is refractory to therapy.\(^1\)

Finally, after the treatment, neither we\(^7\) nor other investigators\(^8\) have found any modifications in the number of CD3\(^{+}\) T lymphocytes or in the distribution of their CD3\(^{+}\)CD4\(^{+}\) and CD3\(^{+}\)CD8\(^{+}\) subsets.

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JW Semple and J Freedman