Increasing level of CD56+ T-cells in peripheral blood in sarcoidosis

To the Editors:

We read with interest the recent paper by KATCHAR *et al.* [1] reporting the characterisation of natural killer (NK) cells and CD56+ T-cells in sarcoidosis patients. The authors observed that, in the lung of patients with pulmonary sarcoidosis, NK cells have a distinct phenotype. They produce cytokines and participate actively in the T-helper (Th)-1-like inflammatory response. In addition, although they did not find any difference in the NK cell number between sarcoidosis patients and control subjects, the authors found an elevation of CD56+ T-cells in the peripheral blood (PB) of sarcoidosis patients. CD56+ T-cells are large granular lymphocytes with a significant proportion of CD4-CD8- cells or γδ T-cells, and, to our knowledge, this is the first study in which such expansion of CD56+ T-cells in PB is described in sarcoidosis.

In a recent prospective study, we analysed the NK cells and CD56+ T-cells content in PB from 32 patients with pulmonary sarcoidosis and from 18 healthy volunteers by flow cytometry.

In sarcoidosis patients, we found that the lymphocyte count was lower ($1{,}312 \pm 583 \cdot mm^{-3}$) than in control subjects ($2{,}439 \pm 481 \cdot mm^{-3}$; $p<0.0005$), the NK cell count was identical ($215 \pm 139 \cdot mm^{-3}$ *versus* $281 \pm 144 \cdot mm^{-3}$; $p=0.1$) although the percentage was significantly different ($18 \pm 10\%$ *versus* $11 \pm 5\%$; $p=0.004$), and finally both the CD56+ T-cell count and percentage were higher in sarcoidosis patients than in control subjects ($158 \pm 122 \cdot mm^{-3}$, $12 \pm 8\%$ *versus* $53 \pm 45 \cdot mm^{-3}$, $2 \pm 1\%$; $p<0.0001$).

With respect to the upper limit of normal CD56+ T-cell count (mean + 2SD), the patients could be separated into two groups: 1) group A (n=15) comprising patients with elevated CD56+ T-cell counts ($269 \pm 97 \cdot mm^{-3}$); and 2) group B (n=17) comprising patients with a normal CD56+ T-cell count ($63 \cdot mm^{-3}$). Interestingly, the patients in group B had a lower lymphocyte count ($964 \pm 331 \cdot mm^{-3}$) than the patients of group A ($1{,}527 \pm 388 \cdot mm^{-3}$; $p=0.0002$) and a lower CD8+ T-cell count ($173 \pm 102 \cdot mm^{-3}$ *versus* $436 \pm 165 \cdot mm^{-3}$; $p<0.0001$). However, these parameters did not correlate with the physical characteristics (*i.e.* sex and age), the clinical presentation (disease activity and radiographic staging) and the evolutionary trend of patients of the two groups.

CD56+ T-cells are cytotoxic cells that play an important role in the Th-1 responses [2]. Their expansion is observed in the elderly and in pathologies involving chronic activation of the immune system, such as viral infections, rheumatic and autoimmune diseases or tumours [3]. For instance, recently, Behcet's uveitis was found to be associated with an elevation of CD56+ T-cells in PB, which returned to normal after treatment [4, 5]. Yet, in sarcoidosis, the functional significance of increased CD56+ T-cells is unclear.

Therefore, our results indicate that the polymorphism of the immune response in sarcoidosis and the clinical presentation are independent, underlining the fact that the status of peripheral CD56+ T-cells does not reflect the activity of sarcoidosis. However, together with the findings of KATCHAR *et al.* [1], our results indicate that studying the phenotypical, functional and cytokine production changes of these cells in peripheral blood (and in the sarcoid granuloma), before and after treatment, will be extremely informative.

J-M. Naccache*, M. Kambouchner[#], P.O. Schischmanoff[¶,+] F. Baran-Marszak[+], M. Raphaël[+,§], R. Fagard[¶,+] and D. Valeyre*[,+]

Service de Pneumologie,, [#]Laboratoire d'Anatomie pathologique, and, [¶]Laboratoire de Biochimie et de Biologie moléculaire, Hôpital Avicenne, and, [+]Université Paris 13, UPRES-EA 3406, Bobigny, and [§]Laboratoire d'Hématologie et d'Immunologie Biologiques, Cytogénétique, INSERM E109, CHU Bicêtre, AP-HP, Paris, France.

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