To the Editor:

The question of whether the initial eosinophilia in case 2 of our report could have been due to Aspergillus infection, perhaps allergic bronchopulmonary Aspergillus (ABPA), can be answered with reasonable certainty. In our opinion the patient did not have specific evidence for the diagnosis of an Aspergillus infection. Cultures for clinically significant Aspergillus are identified in two to six days. 1 Aspergillus is a ubiquitous organism, 2 and identification over three weeks following set up of cultures is, in our opinion, most likely a contaminant. This interpretation is corroborated by other data including: 1) negative specific serum immunoprecipitins for Aspergillus, 2) no evidence of Aspergillus or ABPA on lung biopsy, 3) repeated negative sputum cultures for Aspergillus, and 4) no evidence of Aspergillus at autopsy.

In a patient with the widespread disease that our case 2 presented, repeated negative sputum cultures for Aspergillus should make one wary of the diagnosis of ABPA.

On the other hand, the evidence for coccidioidomycosis is, in our opinion, quite convincing. Negative skin tests and serologies performed during the first week of illness do not exclude the diagnosis of coccidioidomycosis. Seventeen percent of skin tests are negative during the first week of clinical illness 3 and complement fixation and immunodiffusion tests are known to be delayed in their conversion as compared to other serologic tests. 4 Conversion of serologic titers at a little over one month following onset of clinical symptoms supports the diagnosis of coccidioidomycosis.

While skin tests and serologies are frequently helpful in diagnosing coccidioidomycosis, they must be used properly and occasionally (as in this case) become positive too late in the clinical course to be of use. We disagree with the philosophy of blindly increasing doses of steroids and cytotoxic drugs in the absence of a well established diagnosis. A complete evaluation, even to the extent of repeat lung biopsy (when the diagnosis is obtainable by less invasive means) is necessary to ensure proper care when faced with the clinical problem of a patient who is deteriorating on immunosuppressive therapy with no known diagnosis.

Most patients who develop eosinophilic types of pulmonary hypersensitivity reactions have histories of atopy and may have elevated IgE levels for a variety of reasons. 5 In this case, no specific immunoprecipitins were identified and we are unable to comment any further on the significance of this patient's elevated IgE level.

As with all patients transferred to Stanford University for medical care, this patient's medical records were reviewed. Unfortunately, they were incomplete, as noted by Dr. Douglas. Nevertheless, the additional information she provides is interesting and helps further support our conclusions. We thank her for drawing it to our attention.

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REFERENCES


To the Editor:

Diagnostic bronchoalveolar lavage (BAL), with the determination and enumeration of the recovered nucleated cells, has gained wide acceptance in the evaluation of alveolar and interstitial pulmonary diseases. 1 Evolutive sarcoidosis, for example, is characterized by the exudation of activated T-helper cells. Recently we have had the opportunity to observe an unusual increase in NK cells, the "third" or "null" lymphocyte subpopulation, in an aged patient with sarcoidosis.

CASE REPORT

An 80-year-old caucasian woman was admitted because of mental deterioration and confusion. No specific complaint was elicited. Fine crackling pulmonary rales were heard at both bases. The biology was unremarkable; acute phase reactants, serum calcium, alkaline phosphatase, gamma-glutamyl transferase and angiotensin converting enzyme were normal. Gammaglobulins were mildly depressed at 630 mg/L. Routine chest x-ray and computed tomographic examinations disclosed hilar adenopathies and a mild bilateral fibrosis. Functional respiratory tests could not be performed. As shown in Table 1, NK cells as determined by anti-CD16 monoclonal antibodies "a" were markedly increased in BAL and marginally in peripheral blood. Bronchial biopsy was negative. Multiple adenopathies were observed at mediastinoscopy, and histology revealed typical noncaseating granulomas.

DISCUSSION

In normal people, NK cells are very few in BAL samples. 4 Our experience in diseased patients is limited, but NK cells did not exceed 12 percent (n = 6, m = 3.8; range 0 to 12). In our patients, 63,740 NK cells/ml of BAL fluid were found. Great care must be exercised in generalizing the data from a single case. However, it raises fruitful hypotheses. NK cell infiltration could be the hallmark of sarcoidosis in old age, the more so as the null cell compartment is expanded in aging. 5

Alternatively, NK increase in BAL could probe quiescent pulmonary sarcoidosis, the clinical picture in our patient. Indeed, NK cells exert suppressive effects on T and B lymphocytes. 6 In the present case, the association of sarcoidosis with NK cells could have been coincidental. However, no explanation can be found. Our patient did not display any symptoms of another disease, such as acute viral

| Table 1—Cell Subpopulations in Peripheral Blood (PB), Ficol-Paque Isolated Mononuclear Cells (PBMC) and Bronchoalveolar Liquid (BAL) in an Aged Patient with Silent Sarcoidosis. |
|-----------------------------|--------|--------|
|                              | PB     | PBMC   | BAL    |
| cell count/µl                | 9100   | 314    |
| percentage of neutrophiles   | 60     | 2      |
| lymphocytes                  | 19     | 6      |
| monocytes                    | 10     | 50     |
| immunofluorescent subsets %  |        |        |
| MoAb                      | Specificity | Predominant | Reactivity |
| OKT3                        | CD3    | pan-T   | 44      |
| OKT4                        | CD4    | TH      | 20      |
| OKT8                        | CD8    | TS/C    | 21      |
| Leu 11                      | CD16   | NK      | 23      |
| OKM1                        | CR3-CD11 | NK, PMN, mono | 25 |
| OKM3                        | —      | mono    | 44      |
| OKla                        | monomorphic | B, mono, activated T | 38 |
| HLA-DR                      |        |        |
| Leu 16                      | CD20   | B       | 8       |

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disease or leukemoid NK lymphocytosis. Sarcoïd-like granulomas are often observed in voisinage of tumoral foci, but neoplasia is more frequently associated with NK depression.

Determination of the NK subset in BAL clearly deserves further studies in pulmonary diseases.


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Second, while the laboratory staff have made genuine efforts to curtail cost by refusing specimens of sputum already collected, they overlook another important fact, a significant amount of money and time have already been spent by the nursing and courier staff to collect and transport the sputum specimens, especially when the specimen is produced by aerosol induction. In other words, while the laboratory authorities have been trying to reduce the cost in the laboratory, the overall expenses for the hospital or institution is the same and, by refusing specimens which are already collected, the money and time spent already will be wasted. It is also prudent to consider that, unless the laboratory has genuinely reduced the other expenses by reducing the personnel or other operating expenses in the laboratory, the unit cost per specimen processed, or unit cost for positive culture obtained, will be even more, not less, by refusing some specimens already collected; this point has been excellently analysed by Sbarbaro in his editorial.

Third, the dangers that may accumulate by the laboratory personnel action in directing or controlling the clinicians role and privileges in managing the patients should be considered. After all, the clinician has direct and detailed contact with the patient and will be aware of the possibility of tuberculosis and therefore has ordered the specimen of sputum to consider or at least to rule out a diagnosis of tuberculosis. Unless the laboratory has some evidence to show that the physician or his colleagues are indiscriminately ordering a multitude of specimens, the laboratory has no justification to reject any specimen of sputum collected from the patient. If the laboratory has evidence of overuse by the clinicians of limited laboratory facilities, an effort to educate the clinicians is in order. But at any stage, refusal of a specimen already collected is out of order and likely not in the best interest of the patients and their medical care.

Finally, the modest danger of the superficial take home message from this study should be noted. The dangers of missed or delayed diagnosis with the resulting economic impact on the patient, their contacts in society and the extra costs of treatment and hospitalization with the incorrect diagnosis, all resulting from the physicians' getting a wrong message, should be avoided. While cost containment and avoidance of wastage should be encouraged, they should be carefully weighed against the other benefits and losses for the most important aspect, the health care of the patients.

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