This report describes cytoplasmic abnormalities in monocytes from patients with AIDS. Visualized on Wright-stained peripheral blood smears, these abnormalities were not found in normal monocytes, monocytes from patients receiving chemotherapy, monocytes from patients with monocytosis related to non-HIV viral or bacterial infection, or monocytes from patients with monocytic leukemia (French-American-British [FAB] classification M4 or M5). The cytoplasmic abnormalities were detected on panoptically stained blood smears using an ordinary light microscope. As such, a medical technologist and pathologist can detect them as a part of reviewing peripheral blood specimens that are flagged by modern hematology analyzers.

Materials and Methods

As enumerated in [T1], from a total of 275 samples of peripheral venous blood samples anticoagulated with EDTA (no more than 2 hours old), peripheral blood smears were made in an automated slidemaker-stainer (Sysmex M) and stained with a modified Wright stain. In the study, 82 of the 275 samples were obtained from patients who were HIV positive by Western blot. Other samples used as controls for the study were not subjected to Western blot analysis. At the time that blood smears were being reviewed microscopically, the author was not aware of the CD4 values of the blood samples from which the slides were made. Of the 82 HIV-positive patients, 34 had CD4 counts less than 200/µL (0.2 × 10^9/L) and fit the current definition for AIDS.

In 48 patients with abnormal lymphocyte subsets, CD4 counts were greater than 200/µL (0.2 × 10^9/L).

For controls, blood smears were obtained from 66 hematologically normal persons and from 43 patients whose peripheral blood specimens were flagged by the analyzer for monocytosis (monocytes 2,000/µL [0.2 × 10^9/L] or greater). For
examples containing young or immature monocytes, specimens were obtained from 22 newborn infants, 12 of whom had acute bacterial infections and were hospitalized in a neonatal intensive care unit.

Blood smears were also obtained from 3 patients with chronic monomocytic leukemia (CMML), 12 patients with acute myelomonocytic leukemia (FAB M4), 4 patients with acute monocytic leukemia (FAB M5), 29 patients with infectious mononucleosis, and 14 patients who were receiving a variety of different types of chemotherapy for solid tumor malignant neoplasms. These chemotherapies included 5-fluorouracil, irinotecan, doxorubicin, cyclophosphamide, etoposide, and paclitaxel, given alone or in various combinations.

All specimens were viewed under an ordinary light microscope and photographed with a Orthomat (Leica Microsystems) photographic microscope under oil immersion, using Kodak Technical Pan film and simultaneous Kodak 57A and 58 green filters. These filters markedly intensified the cytoplasmic fibrils and their patterns in monocytes. Black and white prints of photomicrographs were scanned, and cytoplasmic fibrillar patterns were accentuated using computer software (Photoshop, Adobe Systems) to enhance brightness and contrast. Under these conditions, cytoplasmic fibrils appeared sharp and distinct.

**Results**

In virtually all monocytes from hematologically normal persons, newborns, patients with non-HIV viral or bacterial infection, and patients with monocytic leukemia, there was an orderly web pattern of coarse fibrils in the cytoplasm. In senescent-appearing monocytes, the web pattern was often found in 1 or 2 quadrants of the cell, contrasting with the more widespread web observed in young monocytes.

As shown in [T2], 34 HIV-positive patients had CD4 counts less than 200/µL (0.2 × 10^9/L) and fit the current criteria for clinical AIDS. Of these 34 patients, 29 (85%) had 90% or more monocytes that lacked cytoplasmic webs, and 5 had monocytes that contained cytoplasmic webs. By using the Fisher exact test and Pearson chi-square test, these figures showed P < 0.0001. The odds ratio (OR) was 11.6, calculated as (5 × 16) ÷ (32 × 29) = 0.0862; OR = 1 ÷ 0.0862 = 11.6.

Monocytes lacking cytoplasmic webs had a characteristic light microscopic appearance. Rather than the orderly web pattern of cytoplasmic fibrils found in normal monocytes and in monocytes
from a variety of non-HIV disorders, monocytes lacking webs displayed a distinct disorganization of cytoplasmic fibrils \[2\]. They seemed to course in various directions throughout the cytoplasm, appearing haphazard. In persons without HIV infection as well as in those with HIV, the web pattern was observed infrequently in monocytes that had 1 or more cytoplasmic vacuoles. Also, the cytoplasm of monocytes lacking webs often appeared paler than normal monocytes and sometimes displayed a yellowish tint with patches of pale lavender.

In monocytes lacking cytoplasmic webs, fibrils appeared thin, delicate, short, and fragmented. In 2% to 3% of these cells, 1 or more fibrils formed a loop or figure-8-like structure \[2d\]. Finally, pink cytoplasmic granules found in normal monocytes and in monocytes from patients who did not have AIDS were decreased or absent in monocytes that lacked webs. In this study, monocytes in patients with AIDS did not appear to have an abnormal increase in the number of cytoplasmic vacuoles.

Occasionally, intermediate-sized lymphocytes containing 1 or more cytoplasmic granules displayed small focal areas of a web pattern of cytoplasmic fibrils similar to those found in normal monocytes. This web occurred in hematologically normal persons and in HIV patients without clinical AIDS. It also occurred in patients with AIDS whose monocytes lacked a web. In all patients, small and large atypical lymphocytes lacked a cytoplasmic web. Morphologically, neutrophils, eosinophils, and basophils from HIV-positive patients and from non-HIV patients were indistinguishable.

**Discussion**

For some time, it has been suspected that monocytes have a key role in AIDS and in the dissemination of the HIV throughout the body.\[4-12\] Yet, there have been few if any studies describing morphologic abnormalities of human peripheral blood monocytes in patients with AIDS.\[13\]

The information contained in the present study suggests that in patients with AIDS, monocytes have a distinctive abnormality of cytoplasmic fibrils not found in monocytes from hematologically normal or leukemic patients, in patients with monocytosis, or in patients receiving chemotherapy. To the best of this author’s knowledge, no mention has been made of these cytoplasmic fibrils either in normal human monocytes viewed under the light microscope\[14\] or in HIV-infected human monocytes viewed ultrastructurally.\[13\]

In this study, if monocytes from an HIV-positive patient lacked cytoplasmic webs, the chances were 85% that the patient had clinical AIDS.\[1\] This contrasts with 33% of patients, or 16 of 48, who had no cytoplasmic webs in monocytes and no clinical AIDS by current criteria.\[1\] The odds ratio of 11.6 indicates that if an HIV-positive patient’s monocytes lack cytoplasmic webs, the chance of the patient having clinical AIDS is 11.6 times that of not having clinical AIDS (\(P < .0001\)).

**Conclusions and Future Studies**

This study indicates that cytoplasmic abnormalities of monocytes from patients with AIDS are distinctive and not found in persons without disease or in monocytes from other disorders. As a result, they constitute new criteria for cytologic abnormalities in monocytes from AIDS patients and should be evaluated in double-blind studies using additional patients. Possibly, the cytologic abnormalities could be used by the medical technologist and pathologist as a part of a triage mechanism to screen large numbers of blood smears for AIDS and thereby help to determine which samples require further evaluation. At present, serial HIV titers and CD4 determinations are 2 variables used to follow the clinical course of patients with AIDS. Future studies will be required to ascertain whether the observations described can also be used to monitor the cellular response to antiretroviral therapy.

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