Declining Immunoglobulin A Production in Prostates of Men with AIDS

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We studied immunoglobulin A production (IgA) in prostates of men with AIDS. Prostate sections from AIDS patients and human immunodeficiency virus-negative men were stained for IgA with immunoperoxidase. Prostate sections from nondiseased men were positive for IgA, while prostate sections from AIDS patients were essentially negative for IgA. Diminishing secretory IgA production may represent a characteristic of AIDS.

Human immunodeficiency virus (HIV) is often sexually transmitted. Because of this, understanding the role of the genitourinary organs which harbor and disseminate this virus may help elucidate the natural history of HIV infection and the development of AIDS. In men with AIDS, the prostate has been identified as a reservoir of HIV (5, 7, 9). As in many organs which maintain glandular mucosa, the prostate produces secretory immunoglobulin A (IgA) (2, 3, 6, 12). The role of IgA in the prostates of men with AIDS has not been studied in depth. We undertook this study to identify the presence and distribution of IgA in the prostates of men who died of AIDS and to determine if there was a difference in prostatic IgA production between men with AIDS and a nondiseased population.

We took care to assure that infection with HIV and development of AIDS were the fundamental differences between the two groups of men studied. Men who died of AIDS were identified among autopsy cases between 1987 and 1989. For comparison, we sought a nondiseased population which could not have been exposed to HIV. We used autopsy cases performed on men who died of noninfectious causes in 1976. This population was chronologically not at risk for HIV infection.

Sections from the prostate were used. Immunohistochemical analysis was done by an indirect immunoperoxidase method using the Ventana NEXES system with prediluted rabbit polyclonal IgA antibody (1.65 μg/ml; Cell Marque Corporation, Austin, Tex.). The chromogen was diaminobenzidine.

The resulting slides were reviewed in a double-blind fashion by the authors. The presence of IgA in the mucosal cells of the prostatic ducts or acini was determined by the presence of crisp, dark brown, distinct diaminobenzidine staining in the cytoplasm of the cells. Prostate sections were evaluated as positive or negative and sorted according to the HIV status of the subject. The resulting data were compared in a standard chi-square test. Differences in age were tested by using a standard t test.

Thirteen men who died from AIDS were study subjects. They ranged from 30 to 52 years old (mean age, 38 years). The patients died from complications of AIDS, particularly multiple opportunistic infections. The nondiseased population was matched to 13 men, 13 to 58 years old (mean age, 40 years). They died from noninfectious causes. There was no statistically significant age difference between the AIDS and non-AIDS populations.

Histologically, prostates from nondiseased men showed diffuse and intense staining for IgA in the glandular epithelium. By contrast, prostates from men with AIDS showed insignificant or no staining for IgA. The prostate sections of only five men with AIDS had convincingly positive IgA staining, while those of 12 of the nondiseased men had crisp, strong staining for IgA. This distribution of positive staining for IgA in healthy men, contrasted with the negative staining for IgA in men with AIDS, was statistically significant (P < 0.006).

Secretory IgA is a widely distributed immunoglobulin in healthy individuals. It is produced by the mucosal surfaces of many organs with secretory epithelium. Infection with HIV and progression to AIDS can reduce IgA production in these organs. IgA production in the salivary gland decreases as HIV infection progresses to full-blown AIDS (4). The concentration of IgA from epithelial lining fluid of the lung may greatly diminish in patients infected with HIV (8). In the gastrointestinal tract, there is a decrease in the mucosal elaboration of IgA (11). In the female reproductive tract, infection with HIV has also been associated with a decreased concentration of IgA in cervicovaginal secretions (1).

We found a comparable pattern of declining IgA production in prostates of men who died from AIDS. It is possible that the difference is due to the progression of HIV disease, and this process of diminishing IgA production in the secretory organs which normally manufacture IgA may be a characteristic of the pathobiology of HIV.

Interestingly, there appears to be an exchange of humoral immune components in the prostates of men with AIDS. An immunoperoxidase study of the secretory component (SC) of the prostate and reproductive tract showed that men who died of AIDS had increased levels of SC compared to those of HIV-negative men (10). This report initially appears to contradict our findings. However, epithelial mucosal cells typically produce more SC than IgA, so unbound SC is usually secreted in the prostate. Moreover, mucosal synthesis and translocation of SC appear to be independent of the presence of IgA (13). Thus, the appearance of elevated free SC in patients who died of AIDS may represent either a relative increase due to the loss of secretory IgA or an actual increase that occurs as the immune system attempts to compensate for lost IgA by up-regulating SC production to collect more of the diminishing antibody.

In summary, there appears to be a systematic pattern of HIV activity in mucosal organs which produce IgA, including salivary glands, lungs, the gastrointestinal tract, the female repro-
ductive tract, and as we have found, the prostate. This effect includes eventual attenuation of IgA production in these organs. The additional significance of this finding for the prostate is that the decline of IgA production may contribute to the transmission of HIV. Overall, this pattern of secretory IgA loss appears to be a significant development in the progression of AIDS.

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