CURRENT CONCEPTS:
ACQUIRED IMMUNE DEFICIENCY SYNDROME

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Introduction

Patients presenting with Kaposi's Sarcoma (KS), opportunistic infections and immune deficiency were recognized, as early as 1978, to represent a distinct clinical entity. It was named “Acquired Immune Deficiency Syndrome” (AIDS). The opportunistic infections in these patients varied and included pneumocystis carinii pneumonia, cryptococcosis, toxoplasmosis, cytomegalovirus infections (CMV) and atypical mycobacteriosis, Esophagitis due to candida albicans, herpes simplex virus (HSV) and CMV was also present in some patients. The immunological deficiency was later discovered to be a specific defect in cell mediated immunity.

Centre for Disease Control (CDC) defines a case of AIDS as “a disease, at least moderately predictive of a defect in cell mediated immunity, occurring in a person with no known causes for diminished resistance to that disease.” The disease has been reported predominantly in homosexual males (75%), intravenous drug abusers without a history of homosexual activity (13%), Haitians with no history of homosexuality or drug abuse (6%), hemophiliacs (0.3%) and persons in none of the above categories (5%). The diagnosis of AIDS is based on clinical manifestations which may range from absence of symptoms, persistent low-grade fever, night-sweats, unexplained weight loss of more than 10 lbs. in two months and persistent generalized lymphadenopathy. Specific diseases namely tuberculosis, oral candidiasis, herpes zoster that cause or result from immunodeficiency may also be present.

Pathogenesis

The Etiology and Pathogenesis of AIDS is still not completely understood, although there is a consensus among researchers that it is a disorder of immunoregulation, specifically involving the cell mediated immune function.

In June of 1981, CDC reported an alarmingly high occurrence of KS and opportunistic infections in previously healthy male homosexuals with a clustering in New York and California. The opportunistic pathogens included pneumocystis carinii, candida albicans, and mycobacterium tuberculosis. The other most predominantly associated infections were those of CMV and Herpes Simplex Virus, as evidenced by elevated serum antibody titres for recent infections. Almost all cases exhibited profound immunosuppression, selectively of T. lymphocytes. A marked reduction of number of circulating T-helper cell with a normal or elevated proportion of T. suppressor cells and a reversal of Helper/Suppressor cell ratio had been reported.

A viral etiology of AID Syndrome has been entertained in previous literature. There is a high prevalence of CMV infection in male homosexuals. An elevated titre of antibodies to CMV indicating a previous exposure is noted in 94% of homosexual males. It is well known that acute CMV infection results in a profound and prolonged immunosuppression of T. cells. Other human viruses belonging to the DNA group and having a high preponderance of infection in homosexual males are Epstein Barr, (EB) Herpes Simplex type 2 (HS2) and hepatitis B viruses. (HBV) These viruses have been considered to have a possible oncogenic role, namely the association of CMV with KS, EB with Burkitts lymphoma and nasopharyngeal carcinoma, HS2 with carcinoma of uterine cervix and HBV with hepatocellular carcinoma.

Intravenous drug use is also very common in populations that are at risk of AIDS. It is reported in 86.4% of homosexual and bi-sexual males when compared to 14.9%, heterosexual group. Drugs like amyl nitrate, isobutyl nitrite and marijuana may have some in vivo T. cell depression.

Recurrent venereal infections commonly seen in promiscuous and homosexual males require repeated antibiotic treatments and some of these, i.e. tetracyclins, metronidazole, in turn might cause immunosuppression. The high incidence of tuberculosis in Haitian immigrants requires treatment with drugs like Rifampin, which is known to give rise to immunosuppression in vivo and in vitro.

In a study of disseminated KS in homosexual males Freidman-Kein et al found a significant increase in HLA—DR allele. This allele was also present in homosexual males with the classic KS localized to skin and extremeties. The association of HLA-DR5 allele is also of special interest as it has

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the highest frequency in black (40-50%), Italians (35.8%), Jews (34-20%). These are the groups with highest prevalence of classic KS. Another observation that the occurrence of KS coincides with the outbreaks of opportunistic infections also indicates a close relationship.

To summarize, the etiology of AIDS is probably multifactorial. A viral agent most likely CMV virus, is probable the initiating agent. The population with the likelihood of repeated viral infections and hence a permanent state of immunosuppression, is therefore at a high risk. The immunosuppressive state is made worse by other factors like IV drugs, sperm and recreational drugs. The possible inhalants and mutants and makes patients vulnerable to opportunistic infections. Hence a permanent state with the likelihood of repeated opportunistic infections also indicates a certain genetic predisposition. It is conceivable that a genetically disposed person, with a major defect in cell mediated immunity brought about by a number of factors, is most susceptible to AIDS. The genetic disposition, the presence or absence of multiple diseases and intactness of the humoral arm of the immune system, perhaps determine the outcome of the disease.

**Laboratory Data**

The major findings are:

a. Persistant leucopenia.

b. A decrease in absolute number of circulating lymphocytes.

c. Selective decrease in circulating helper cell population; with an increase in T-cytotoxic suppression cell population.

d. Decrease helper/suppressor cell ratio (N: 1.7 - 2.1) AIDS: < 1.0.

e. Decreased reaction to various antigens in skin testings.

f. Elevated titres to CMV antibodies.

g. Natural killer cells: (NK) in 40% of patients there was complete absence of NK cell activity in AIDS patients with Kaposi's sarcoma. (Normal 0 - 10% of circulating antibodies are NK cells.)

h. Elevated serum immuoglobulins.

**Histopathology and Autopsy Findings in AIDS**

Lymph nodes biopsies in homosexual males with AIDS with clinical, generalized lymphadenopathy have been studied. These reports indicate that the most consistent finding is a generalized reactive hyperplasia of lymph nodes.

Fernandez et al have studied 54 biopsies and found four distinct patterns. The most common pattern was extensive follicular hyperplasia, the next common pattern was a mixed follicular hyperplasia as well as paracortical hyperplasia. Four out of fifty-four patients had a B cell lymphoma. Although a benign reactive hyperplasia is the most consistent finding, occasional lymphomas have also been seen. Autopsy findings have been studied in six patients with AIDS. CMV infections were the most consistent (4 patients). The adrenal glands were involved extensively, one patient had KS and cerebral and myocardial toxo plasmosis. There were a total of three cases KS. In no case, did KS contribute directly to the patient's death; the cause of death was pneumocystis pneumonia. Presence of several disseminated infections has also been reported by the authors.

In Fligiel and Naeim's study a prominent lymphoid atrophy of the thymus gland with marked pauciity of lymphoid follicles was also seen. The spleen and lymph nodes also showed marked lymphocytic depletion.

**Transmission and Precautions**

The epidemiology of AIDS suggest a possible, not yet identified blood borne agent transmitted in a manner similar to hepatitis B virus. CDC had suggested (MMWR 1982, 31: 577-579) that AIDS patients and specimens should be treated as if they were "infectious". Although it is prudent to take all possible precautions to minimize potential risk of AIDS transmission by hepatitis B vaccination, CDC has cleared hepatitis B vaccine as a vehicle of AIDS transmission. After a considerable follow-up of several thousand patients and specimens it was concluded that Hepatitis B vaccination, CDC stated (American Medical News, February 4, 1983), "we can say strongly that hepatitis vaccine does not cause AIDS."

CDC has recommended that the following precautions be undertaken in order to minimize a potential risk to hospital personnel:

1. Use of gloves during drawing blood and direct contact with the secretions.
2. Labelling and bagging of blood specimens.
3. Proper disposal of needles and syringes.
4. Designation of special areas in the hospital for isolation (Example: machine isolation in the dialysis unit).

The above procedures are to be followed in the following groups:

(A) Patients > 60 years with KS. (biopsy proved) or with opportunistic infections.

(B) Homosexuals males, (on strong suspicions clinically), hemophiliacs, Haitian im-
migrants, patients with a history of parenteral drug use with fever which is not readily diagnosed.

**Possible Therapeutic Interventions**

Immune potentiators have been gaining popularity in children as well as adults with immune deficiency syndrome.\(^3\) Trials of synthetic interferon -1 and -2 are being undertaken in AIDS. Thymosin fraction 5—is one of the hormones isolated from thymus to induce maturation of uncommitted bone-marrow lymphocytes into mature T lymphocytes. This has been tried in two patients with CMV and KS with some encouraging results. Both thymosin fraction 5 and synthetic thymosin \(\alpha\)-1, have shown promise in malignant gliomas, renal cell carcinomas and in correcting immunological disorders in studies performed under the guidance of the National Cancer Institute. (JAMA 1982, 248-807) In Conclusion, the diagnosis of AIDS should be entertained in all patients who are at a high risk for developing the disease. Cases in whom the history and the physical examination lends weight to the suspicion of AIDS, should have a complete laboratory work up including routine tests, assessment of immunological status and skin and lymph node biopsies. Although specific treatment is not available as yet, early recognition will provide the challenging opportunity to discover intervention strategies.

**Bibliography**


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